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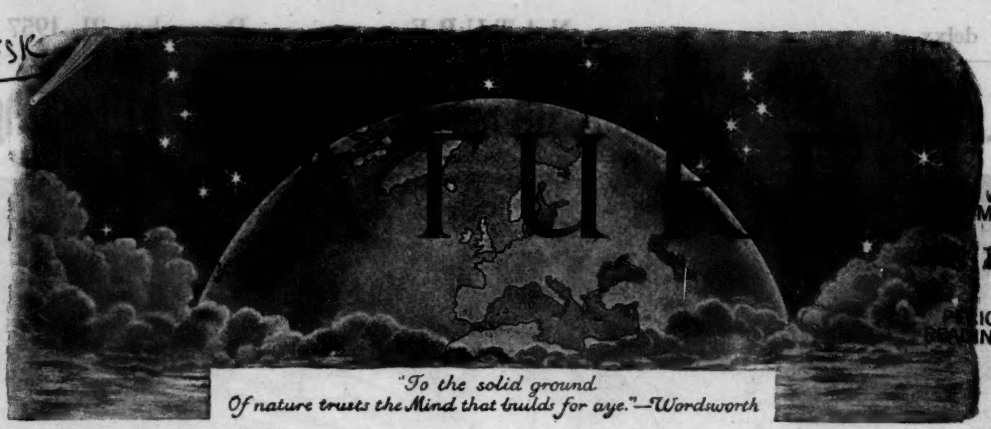

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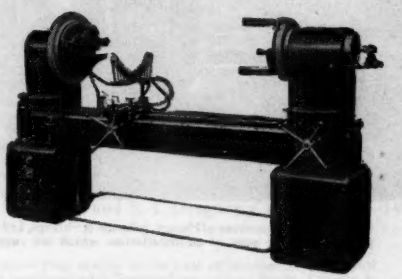

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AGENTS THROUGHOUT THE WORLD

NATURE

No. 4599 SATURDAY, DECEMBER 21, 1957 Vol. 180

CONTENTS

Page

Co-operation in Science, Technology and Industry in the Western World 1377

Sugar Industry in the South Pacific. By Sir Harold Hartley, G.C.V.O., C.B.E., F.R.S. 1378
Some Modern Aspects of Enzyme Research. By Prof. D. D. Woods, F.R.S. 1379
High-Voltage Transmission Systems. By Dr. J. S. Forrest 1379
Teeth of the Aleuts. By F. Taylor Monks 1380
Multichannel Pulse Height Analysers. By Dr. Denis Taylor 1381

Economics of Atomic Power Development in India and the Indian Atomic Energy Programme. By Dr. H. J. Bhabha, F.R.S. 1382
Optical Definition of the Metre. By Dr. H. Barrell 1387
Structure and Functioning of the Nervous System. By Dr. W. K. Taylor 1388

Obituary :
Prof. Heinrich Balss. By Dr. Isabella Gordon 1391

News and Views 1391

Colour Vision. By Dr. W. S. Stiles, O.B.E., F.R.S. 1395
Safety in the Chemical Industry 1397
School Natural History Societies Exhibition. By O. N. Bishop 1399
Dew 1400
Long Ashton Research Station 1400
Enhancement of Vitamin B_{12} Absorption by Substances other than Intrinsic Factor. By Samuel M. Greenberg, John F. Herndon, Edward G. Rice, Edwin T. Parmelee, John J. Gulesich and Edward J. van Loon 1401
An Experiment on 'Telepathy' using Television. By Donald Michie and D. J. West 1402
Noise and the Visual Threshold. By M. G. Bulmer and C. I. Howarth ; Violet Cane and R. L. Gregory ; H. B. Barlow 1403

Letters to the Editors :

Occurrence of the Meta-stable Omega Phase in Zirconium Alloys.—B. A. Hatt, J. A. Roberts and G. I. Williams 1406

Some Properties of Chromium deposited from an Electrolyte containing Fluoride.—N. E. Ryan, F. Henderson, S. T. M. Johnstone and H. L. Wain 1406

Corrosion as affected by a Zone of Metal emerging from the Corrosive.—Dr. P. Hersch 1407

Photographic Densitometry with the Two-Wave-length Method.—Dr. Mortimer L. Mendelsohn 1408

Intramolecular Transfer of Electronic Energy in Dihydro Diphosphopyridine Nucleotide.—Dr. G. Weber 1409

Polarization of Comet Arend-Roland.—Dr. M. K. Vainu Bappu and Dr. S. D. Sinvhal 1410

Crystal Structure of Oximes.—Bodil Jerslev 1410

Spiral Crystals of Meconin.—W. R. Logan 1412

A New Metallic Layer Structure.—J. F. de Wet 1412

Life-time of an Artificial Earth Satellite.—J. A. Fejer 1413

Suppression of Bubbling in Boiling Refrigerants.—Dr. G. J. Minkoff, Floyd I. Scherber and Alfred K. Stober 1413

Differential Thermal Characteristics of Peat.—B. D. Mitchell . . 1414

Modified Method of Carbon Marking.—Dr. P. H. S. Silver . . 1415

Decomposition of Chloro-organic Acids by Fungi.—Prof. H. L. Jensen 1416

Photosensitivity of Hæm Compounds.—Prof. Q. H. Gibson and S. Ainsworth 1416

5-Hydroxytryptamine and Anaphylactic Shock.—Dr. R. K. Sanyal and Dr. G. B. West 1417

Inhibition of Ascorbic Acid Oxidase by Thiourea.—Dr. A. M. Mayer 1417

Metabolism of Pyruvate and α-Ketoglutarate in Virus-infected Mouse Brain.—P. L. Bradley 1418

Ineffectiveness of Selenium in the Treatment of Nutritional Muscular Dystrophy in the Rabbit.—Prof. H. H. Draper 1419

Induction of Mouse Leukæmia with Purified Nucleic Acid Preparations.—Dr. Esther F. Hays, Norman S. Simmons and William S. Beck 1419

Sensitization by Œstradiol to the Production of Experimental Nephrocalcinosis.—Prof. H. Selye 1420

Fluoride Removal by Powdered Dental Enamel from Solutions of Stannous or of Sodium Fluoride.—Dr. Frank A. Smith, Dwight E. Gardner, Dr. Samuel A. Leach and Dr. Harold C. Hodge . . 1421

Denaturation of Fish Proteins.—Dr. A. F. M. G. Luijpen . . . 1422

Role of Structural Degradation in the Loss of Serological Activity of Ovalbumin irradiated with Gamma-Rays.—Hugo Fricke, Charles A. Leone and Wendell Landmann 1423

Transaminases of *Leishmania donovani*, the Causative Organism of Kala-azar.—Dr. A. N. Chatterjee and Dr. J. J. Ghosh . . . 1425

An Effect of Hexylresorcinol on Bacterial Aerosols.—H. M. Darlow and E. O. Powell 1425

A Biochemical Lesion in Congenital, Non-obstructive, Non-hæmolytic Jaundice.—Dr. Julius Axelrod, Dr. Rudi Schmid and Lydia Hammaker 1426

Utilization of 4-Amino 5-Imidazole Carboxamide in Plant Tissues.—Prof. K. V. Giri and P. R. Krishnaswamy 1427

Induction of Immunological Tolerance in Rats to Foreign Erythrocytes.—Dr. G. J. V. Nossal 1427

Antimitotic Activity of 5-Tertiary Butyl Benzimidazolone.—Dr. H. C. Stoerk, R. N. Arison and J. E. Hawkins, jun. 1428

Chemical Nature of Parathyroid Hormone.—Howard Rasmussen and Roland Westall 1429

Toxicity of Erythromycin.—Col. W. D. Tigertt and W. S. Gochenour, jun. 1429

Identical Nature of the Leucocyte Antigens detectable in Monozygotic Twins by means of Immune Iso-Leuco-agglutinins.—J. Dausset and H. Brecy 1430

Ultra-violet Irradiation of Dry Tobacco Mosaic Virus.—Albert Siegel 1430

Subendothelial Space between the Ovarian Interstitial Cell and the Endothelial Lining of the Blood Sinusoids.—Dr. M. De Groodt, A. Lagasse and Prof. M. Sebruyns 1431

Effect of Desiccation on the Eggs of *Simulium damnosum*, Theobald.—Dr. R. C. Muirhead-Thomson 1432

Gonad Temperature and Spontaneous Mutation-rate in Man.—Dr. Lars Ehrenberg, Günter von Ehrenstein and Arne Hedgran 1433

Resumption of Gonadotrophic Function in Pituitary Grafts following Re-transplantation from Kidney to Median Eminence.—M. Nikitovitch-Winer and J. W. Everett 1434

Red-Cell Survival in Familial Hæmolytic Anæmias.—Dr. Robert L. Evans 1435

Effect of Exteroceptive Factors on the Œstrous Cycle of Mice.—M. K. Whitten 1436

The Genus *Cypraea*.—Alison Kay 1436

A Method for concentrating Pollen Grains and Small Fossil Remains from Fibrous Peats and Moss Polsters.—D. M. Churchill . . 1437

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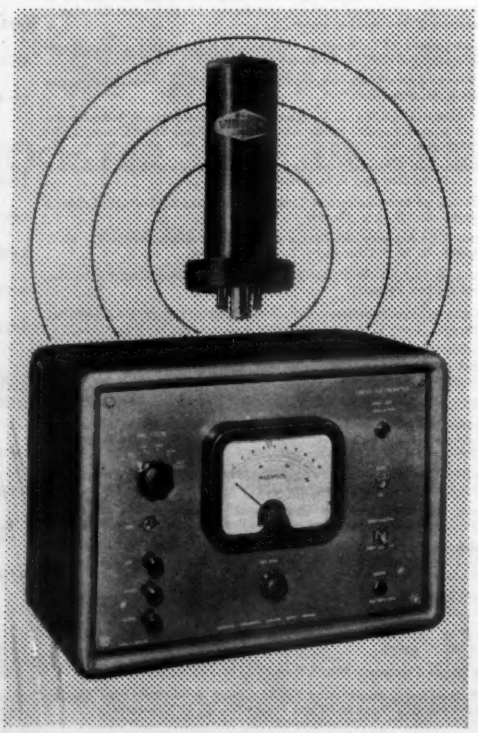

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CO-OPERATION IN SCIENCE, TECHNOLOGY AND INDUSTRY IN THE WESTERN WORLD

THE elaboration of a philosophy of security could be an important factor in securing smooth and effective Anglo-American co-operation, not merely in the exchange of information, but also in the many other directions in which savings in scientific and technological man-power and in material resources are possible. Such collaboration, to be successful, must be really desired by both sides, as it was during the War; it must be based on something more positive than the fear of technical advance in other countries. That is one reason why it is important that confidence should be felt in British security measures. It is also a reason why everything possible should be done to see that British organization for research and development is as efficient as possible, and especially for seeing that full use is made of our opportunities for technological advance. Achievements like Calder Hall are not to be expected every year, but high industrial productivity could be a significant factor in leading the United States to seek closer scientific and technical co-operation with Britain. Next, it must be remembered that to be really effective even for defence purposes, co-operation may well have to cover the whole field of science and technology. Academic research and industrial research may be involved as well as that in Government establishments.

Partly in consequence, there are two further considerations. If much waste of man-power is to be avoided, flexibility is of over-riding importance. The nature of the co-operation required will vary from field to field: sometimes formal arrangements will be necessary; elsewhere informal contacts will suffice between groups of people at different levels. This may well apply particularly in the planning in advance which is essential in all effective research.

This latter consideration is one reason why it is so important to establish confidence and understanding as widely as possible, for without that confidence and understanding neither party will readily accept the risks which are inherent in exchanging views at an early stage, without which effective co-operation in attacking a problem is impossible. The precedent of the Geneva Conference on the Peaceful Uses of Atomic Energy suggests that where scientific issues alone are involved, it should not be difficult to secure effective co-operation; but professional institutions in both countries could do more to promote the extension of co-operation through the existing channels as well as in other ways. On the American side, a valuable article by Dr. W. A. Noyes, jun., in the *Bulletin of the Atomic Scientists* of September 1957, arguing for a scientific foreign policy, pointed out how scientists could support just such a broad policy as President Eisenhower and Mr. Macmillan have recently indicated. Even at the highest level, scientists have some responsibility for seeing that those making decisions of policy have sound advice on scientific matters.

At an intermediate level, dealing with technical assistance or the technical aspects of defence problems, scientists are often official delegates, and, as Dr. Noyes points out, decisions frequently involve scientific matters as well as broad matters of policy. In the United States, the National Academy of Sciences and the National Research Council and the great technical societies are the main bodies called upon for advice. In Britain there is the Advisory Council on Scientific Policy and the Research Defence Policy Committee, while the Lord President of the Council is advised by the four committees of the Privy Council, to which the Department of Scientific and Industrial Research, the Medical Research Council and the Agricultural Research Council and the Nature Conservancy are responsible, with the Minister of Power and the Atomic Energy Authority now standing a little outside and responsible to the Prime Minister.

Doubts have frequently been expressed in recent years as to the effectiveness and appropriateness of this structure, particularly in respect of the Lord President's office, and there would certainly appear to be reason for some fuller inquiry into the whole question. Quite apart from its bearing on Anglo-American co-operation, Britain's research effort should not be expected to be handicapped indefinitely by the inadequacies and inefficiencies of organization manifest in the past few years. This organization, moreover, is concerned with the third more limited level distinguished by Dr. Noyes, dealing with problems mainly of interest to scientists themselves, which in the United States are mostly handled officially by the National Academy of Sciences and the National Research Council. At all three levels, scientists are needed who are versed in the rudiments of diplomacy, familiar with and sympathetic towards other peoples and their cultures, and prepared to give the time to represent their country at international meetings and on missions overseas.

Here we touch on a facet of the educational question, for obviously co-operation will be smoother if the universities and colleges of technology of Britain provide graduates whose training has made them alive to wider issues; they must be capable of taking their place effectively in a team, not simply of fellow experts in their own field, but also of experts in different branches of science and technology and from other walks of life. That is an essential step in the cross-fertilization required for effective co-operation in defence or in other fields. Such cross-fertilization must proceed at all levels. Real integration and effective co-operation are not to be secured without much forethought, preparation and effort, sometimes in fields not immediately apparent.

This may well be true of industrial research. Co-operation in defence, as is clear from the joint declaration, involves, at least in principle, some

degree of economic co-operation; and it has already been emphasized that for Britain, at least, effective defence depends on her economic strength. What she can contribute to the common task depends in large measure on the strength and enterprise of her industries, and accordingly on the magnitude of her industrial research and development and the vision with which that is directed. The inquiries on which Prof. C. F. Carter and Prof. B. R. Williams based their report, "Industry and Technical Progress", revealed some shortcomings in this respect which call imperatively for action in the present context.

Even more pertinent, however, are the comments made by Mr. J. H. Dunning in a study of "Anglo-American Research Co-operation and Industrial Progress" contributed last year to the *District Bank Review*, and in a further article in the *Proceedings of the Chemical Society* last June. Mr. Dunning argues that the British industrial achievement needs to be linked with an economic environment more favourable to exploitation; this is now provided by the presence in Britain of firms financed from the United States, the American economy thus benefiting from basic research carried out here. The greatest advantage of Anglo-American co-operation in research, however, is in the opportunity it affords for specialization in stages in production. Mr. Dunning suggests that if British firms, because of great aptitude, concentrated on basic or fundamental research while their American associates developed and commercialized the results, the production and selling technique would in time be made available to the British firms.

Mr. Dunning does not deny that there are dangers in such co-operation, though he regards the United States economy as complementary to, rather than competitive with, the British economy, and he also points out that, if Britain does not take advantage of the close economic and political ties with the United States in this way, other European nations will do so. He insists, however, that Britain must be partners with America and not simply buyers of knowledge. Britain is still among the leading experimental workshops in the world, and, in relation to her size, is the most prolific source of new ideas. The economic environment, however, is much less favourable than that of the United States for the actual commercialization of ideas, and here Anglo-American co-operation can achieve its greatest mutual benefit and perhaps its most decisive contribution to the common defence.

The declaration of common purpose is above all a challenge to thought and effort in which scientists and technologists, as well as industry, have a decisive part. The responsibility does not rest simply on governments and government institutions. Scientists and technologists, through their professional bodies, have to see that the means of co-operation and the organization for research and development as well as for professional and technical training are appropriate to their task. Industry, too, must remember that Britain cannot stand still or rest on past laurels; it must ever seek both new processes and products and new ways and means of co-operating to that end.

SUGAR INDUSTRY IN THE SOUTH PACIFIC

South Pacific Enterprise

The Colonial Sugar Refining Company, Limited. Edited by A. G. Lowndes. Pp. xvii + 500 + 150 plates. (Sydney and London: Angus and Robertson, Ltd., 1957.) 42*s*.

THE Colonial Sugar Refining Co. was founded in 1855, and this book, aptly named "South Pacific Enterprise", is an account of the development of the Company during its century of existence and of much else besides. It is written by a number of authors drawn from both outside and inside the Company, and their contributions have been welded into a continuous story by the editor, Arthur Lowndes, a well-known agricultural economist. There is not a dull page from start to finish as the writers describe so well the growth and activities of one of the leading Australian industries. The lavish use of illustrations, many of them in colour, helps greatly to bring the story to life.

The book opens with the romantic history of the sugar cane, indigenous in the South Sea Islands, introduced from southern Asia to Mesopotamia in historic times, carried thence to the Mediterranean, and finally taken by Columbus in his second voyage to the Caribbean. Although the sugar cane reached Australia from Tahiti in 1817, it was not until the late 1860's that sugar was produced commercially in Queensland. So in 1855 the Company started out under the energetic leadership of Edward Knox, the grandfather of the present chairman, to refine imported raw sugar. Two years later it was hard hit by a slump in sugar prices and only saved by Knox's resolute action, an experience it met again in 1884 and 1894 when his son, E. W. Knox, was in charge.

Throughout the century the Company has a fine record of prudent financial management and continuous development. In the 1860's when sugar was ceasing to be a luxury article and was entering into normal diet, the Company did much to encourage the growing of cane in Queensland and built mills to crush the cane and extract the raw sugar. The slump in sugar prices in 1884 due to the rapid production of beet sugar turned the attention of E. W. Knox, who had succeeded his father in 1880, to the need for scientific research and control. Chemists were brought in to supervise the extraction of the sugar from the cane and its refining, and to control the price paid for the cane at the mills based on its sugar content. An experimental station was started to study the breeding of better varieties of cane with most successful results, and this is only one of the many ways in which the Company has contributed to the efficiency of sugar production in Queensland and New South Wales.

In 1879 the decision had been taken by the Company to grow sugar in Fiji, an enterprise which has had such an important influence on the economic and social future of the two islands. To-day sugar is by far their largest export. Sugar plantations were started and were later divided into small, native-owned farms. Light railways were built to carry the harvested cane quickly to the mills, an experimental station was opened to breed suitable varieties of sugar cane, and to-day there are two agricultural schools where the young Fijians are given a three-

year course of training. Martin Leake described this venture as "the boldest experiment in colonial agriculture during the present century". However, the charming and easy-going Fijians did not take kindly to the exacting task of raising sugar cane, Indian labour was introduced, and to-day most of the farms are in the hands of Indians, who now outnumber the indigenous Fijian population.

Since 1923 all the raw sugar produced in Australia passes into a pool, controlled by the Queensland Sugar Board, which is operated on its behalf by the Colonial Sugar Refining Co. The Company markets and ships the raw sugar that is surplus to home requirements and it thus has world-wide responsibilities. The home market in Australia and New Zealand is supplied from its own refineries with one small exception. The disposal of the two by-products of the sugar mills, megass, the fibre from which the sugar has been extracted, and molasses, the residual liquor, has produced two major expansions of the Company's activities in recent years. The manufacture of wall boards from megass has led to the large-scale production of building materials from hard woods and asbestos, and an extensive chemical industry has been based on molasses as a raw material in a subsidiary company in partnership with the Distillers Company of Britain.

All these developments are typical of the enterprise which has characterized the Company since its early days, thanks to which it became the first major industrial organization in Australia and its original capital of £150,000 grew to £14 million. The book gives a fascinating account of its history and is of special interest in showing the place it occupies in the economic planning of the world sugar industry.

The individual cultivator of sugar, often with a small holding, is exposed to the risks of the weather and world prices. The Company has played a very active part in the national and international agreements which aim at giving reasonable stability to the industry by planned production and marketing, with a margin to allow for development and experiment. One of the most interesting chapters describes the working of the Commonwealth Sugar Agreement of 1951 and the International Sugar Agreement of 1953, showing the value of a large organization like the Colonial Sugar Refining Co. with adequate resources for research and development, and with continuity of policy based on long experience which has benefited alike the cultivator, the consumer and those engaged in this essential industry. HAROLD HARTLEY

SOME MODERN ASPECTS OF ENZYME RESEARCH

Enzymes

Units of Biological Structure and Function. Edited by Oliver H. Gaebler. (Henry Ford Hospital International Symposium.) Pp. xiv+624. (New York: Academic Press, Inc.; London: Academic Books, Ltd., 1956.) 12 dollars.

THIS book is a record of the formal contributions and discussion at a symposium held in Detroit in November 1955. During the past few years there has been an exponential growth in work and interest concerning aspects of enzyme action other than the chemistry and kinetics of the reactions catalysed and the intimate chemical mechanism of the catalysis. It was to these broader fields that the symposium was devoted; the borderlands between enzyme biochemistry on one hand and cell structure, genetics and physiology on the other. The promising, and in some cases dramatic, increase in knowledge has, of course sprung to some extent from technical advances in, for example, electron microscopy, refined spectrophotometry and the induction and use of mutants of micro-organisms.

The symposium ranged over so wide a field that it is impossible to provide a scientific summary. Equally it would be invidious to select contributions for individual comment; all twenty-nine formal contributors are authorities in their respective fields. The sections on the mechanism of enzyme formation (extending to protein synthesis in general) and its genetic control were naturally based mainly on work with micro-organisms. The session on the relationship of enzymes to cell structure emphasized the potentialities of electron microscopy and cytochemistry. Contributions on cellular energy sources centred on the role of hæm compounds. Specific physiological processes considered in enzymic terms included muscular contraction, secretion and re-absorption in the kidney, vision and bioluminescence. A final session discussed the most elusive problem of all—the co-ordinated regulation of enzyme activity.

The book should prove a most valuable and stimulating guide both to research workers and advanced students. The former may be provoked to considering their own problems more from the point of view of the living intact organism; the latter will also find the symposium gives a novel cross-section of biochemistry and a new appreciation of the real outstanding problems.

Verbatim reports of the general discussion are also given. Except in so far as items of factual information are concerned, the reviewer does not find this so successful. It is not possible to transfer to the printed page the atmosphere and spirit of the conference room; a commentary by an informed reporter might have been more effective.

D. D. WOODS

HIGH-VOLTAGE TRANSMISSION SYSTEMS

A.C. Switchgear

By Dr. J. R. Mortlock. Vol. 1: A Survey of Requirements. (Advanced Engineering Textbooks.) Pp. xi+387. (London: Chapman and Hall, Ltd., 1956.) 50*s*. net.

Neutral Grounding in High-Voltage Transmission

By Dr. R. Willheim and M. Waters. Pp. xviii+669. (Amsterdam: Elsevier Publishing Company; London: Cleaver-Hume Press, Ltd., 1956.) 90*s*.

THESE books discuss important aspects of high-voltage transmission systems; the switchgear controlling the system, and the method adopted to earth the neutral point.

Dr. Mortlock's book is the first volume of two on a.c. switchgear. It is intended to give guidance to power system engineers on the problems associated with the determination of switchgear ratings. The second volume will deal with basic design principles.

The book opens with a chapter on circuit theory and conventions, and the two following chapters deal with the calculation of symmetrical and unsymmetrical fault currents and voltages. The methods of calculating fault currents are clearly and logically explained, and the theory is supplemented by data in the form of tables and diagrams which will, in most practical cases, enable the system engineer to make his own calculations with a minimum of labour. Some information on the electrical characteristics of overhead-lines with 'bundle' conductors might have been included with advantage, as on high-voltage systems this type of line is being increasingly used and the line impedance is much lower than that of a corresponding single-conductor line.

Subsequent chapters discuss methods of limiting fault currents; current and voltage transformers; protective gear; the initiation and interruption of arcs; restriking voltages; and the co-ordination of insulation.

In discussing protective gear, the author rightly emphasizes that the necessary measurements should be carried out statically and the simplest of relays used. He is, however, unduly pessimistic about electronic methods, which "are still in their infancy". In the opinion of the reviewer, electronic techniques and semi-conductor devices could at the present time be used for performing the functions of conventional protective gear relays without any decrease in reliability and with advantages from the points of view of space-saving and ease of maintenance.

The author's treatment of the rather difficult subject of the calculation of restriking voltages is excellent, and here again useful data are included on practical circuit parameters.

The final chapter is a useful statement of current views on insulation co-ordination. It includes an account of methods of calculating the probable number of overhead-line flashovers per annum due to lightning. There is still, however, a serious lack of information on the basic data required for such calculations; for example, estimates of the average number of lightning flashes to earth per square mile per annum vary over a range of 5 to 1. Apart from this, the present theory appears to be inadequate, as recent experience on American and British systems operating at around 300 kV. has shown that the actual number of breakdowns due to lightning is several times the value estimated on the basis of service records on lower voltage systems. However, these gaps in our knowledge are questions for further research and do not reduce the value of the book, which can be thoroughly recommended to the power system engineer.

Dr. Willheim and Mr. Waters's book gives a comprehensive and detailed account of neutral earthing practice on high-voltage systems in many countries. The text is divided into two main parts. The first deals with earth faults and earthing methods in general, and discusses the capacitance and impedance of high-voltage systems; transient overvoltages due to switching, lightning and arcing phenomena; interference with communication circuits; and the suppression of earth faults by expulsion tubes, high-speed reclosing switchgear and Petersen coils.

The second and larger part of the book discusses resonant earthing, that is, the earthing of the neutral point through an inductance tuned to resonate with the capacitance of the system to earth—this greatly reduces the magnitude of the current flowing in a short-circuit to earth. The inductance is variously known as a Petersen coil (after its German inventor), an arc suppression coil (in Britain) and a ground fault neutralizer (in the United States). The authors have adopted American terminology in general. This part of the book deals with the theory of operation of the Petersen coil; the effect of power losses and harmonics; de-coupling coils to avoid interaction between circuits; overvoltages; protective relays; and the design testing and commissioning of Petersen coil earthing systems. Finally they give a survey of the extent to which Petersen coil earthing has been adopted in various countries.

The authors have endeavoured "to co-ordinate the large body of accumulated knowledge, and to assess the position with regard to techniques already in existence or gaining in importance", but it is doubtful if they have been successful in this aim. The reader is not presented with a clear picture of the sphere of application of the various methods of neutral earthing. What is one to make, for example, of the statements that "Solid grounding of the neutral has never been given a chance in Germany and nobody there seems to regret this fact" (p. 610), followed by "Altogether the balance of opinion in Germany as far as 400-kV. transmission is concerned has swung towards solid grounding, as it appears to offer more in the way of immediate advantages" (p. 613)? In general, the reader is left with an impression that the authors favour Petersen coil earthing even at the higher voltages. However, many British engineers consider that, although this is an efficient method of earthing for 33-kV. overhead-line systems of moderate size, the disadvantages outweigh the advantages for extensive systems operating above 66 kV.

The general trend for extensive high-voltage systems is now towards solid earthing, even in continental Europe, and the successful operation of the British grid system, which was designed for solid multiple earthing thirty years ago, has undoubtedly had an important influence on practice in other countries.

J. S. Forrest

TEETH OF THE ALEUTS

The Aleut Dentition

A Correlative Study of Dental Characteristics in an Eskimoid People. By Coenraad F. A. Moorrees. Pp. x+196. (Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1957.) 36*s*. net.

THE Orthodontic Department at the Forsyth Dental Infirmary for Children, Boston, Mass., is fortunate in having as its head Dr. Coenraad F. A. Moorrees. His book is a sound research project which, unfortunately, had to be based on a minimum of available material. The present population of the Aleutian Islands consists of some 156 inhabitants. Even with such a paucity of material Dr. Moorrees would seem to substantiate his initial statement that there are two distinct breeding isolates in this small community, namely, Eastern and Western Aleuts. This fact is made abundantly clear by an evaluation of the basic findings on the retention or intensification of basic characteristics, such as facial disharmony, although no satisfactory explanation can be offered.

The section on odontometry and tooth morphology will delight the statistician and dental anthropologist, and the tables of comparative data given at the end of the book bear witness to the thoroughness of the investigator. It is to be regretted, however, that in such an investigation no provision for X-ray examination was made, and much interesting material must have been missed, such as buried or abnormal teeth. Lack of this facility tends to render problematical the value of any assessment of the caries factor, always an interesting study. For the same reason the fascinating condition of taurodontism, which is present in this community, receives only passing mention. Also, the value of the assessment of absent teeth, whether congenital or fortuitous, is obscured by the arbitrary criteria used in the assessment. Surely a tooth is either present or absent, and if the latter is the case the cause is worthy of further investigation. It was noted that the fluorine intake was low.

Tooth emergence, always a readily accessible means of assessing physiological attainment, is discussed without, however, any definite conclusions being reached as to whether or not the differences noted between Whites and Aleuts can be attributed to racial characteristics or environmental factors.

Angle's classification is used as the basis for assessment of mal-occlusion, but due to changed habits of the Aleuts during the last five decades, little of real value was obtained from this study. It is worthy of note that the pattern of periodontal disease in this community is similar to that found in other peoples.

The book is well written, the findings and deductions being well-proportioned, due allowance being made by the author for discrepancies between the two breeding isolates. The illustrations, charts and tables are most helpful in fully understanding the text, and the references are copious.

The author is to be congratulated on his work, and a copy of this book should be in every dental library.

F. Taylor Monks

MULTICHANNEL PULSE HEIGHT ANALYSERS

Multichannel Pulse Height Analysers

Proceedings of an Informal Conference, Gatlinburg, Tennessee, September 26–28th, 1956. Edited by H. W. Koch and R. W. Johnston. (Nuclear Science Series—Report No. 20. Publication No. 467.) Pp. xi+205. (Washington, D.C.: National Academy of Sciences—National Research Council, 1957.) 2 dollars.

ONLY a decade ago multichannel pulse height analysers were a novelty used by a few nuclear physicists in investigating the spectral emissions of radioactive substances. To-day, many types are in regular commercial manufacture, and almost every laboratory concerned with nuclear physics, radiochemistry or nuclear energy work has at least one of these equipments and requirements for several more. The multichannel pulse height analyser has, in fact, become an essential tool for nuclear research and development.

To the uninitiated the sorting of pulses according to their height may not appear to be a difficult problem, but because of the statistical nature of the phenomena under investigation, the wide range of pulse rates encountered, the extreme variation in pulse height and the high degree of accuracy and stability required, there are many difficulties. An authoritative publication on these and related matters has been lacking for some time, and so designers and users of multichannel pulse height analysers will welcome this new volume summarizing the proceedings of an informal conference on this subject held at Gatlinburg, Tennessee, during September 26–28.

The book is divided into four parts: the statement of the problem; systems; computer techniques; and calibration, *xyz* recording and future trends. Each of the four parts is prefaced by a chairman's statement (a valuable feature) summarizing the more important contributions, and apart from the written versions of the individual lectures, the publication also summarizes the ensuing discussion.

The first section of the book opens with a statement by P. R. Bell, for ten years a designer as well as a critical user of these instruments, who discusses the use of multichannel analysers in the analysis of beta and gamma spectra and indicates some of the main design problems. F. Axel contributes the second lecture, and he describes the various radiation and particle detectors used in association with these analysers, and considers, in particular, the pulse shapes encountered and their amplitudes. The later lectures in this first part of the book deal with the important subject of pulse shaping. Altogether this first section forms a most valuable introduction to the whole subject.

The second part of the book is concerned with 'systems'. At the present time the trend in the design of these analysers is away from systems employing multiple voltage discriminators. Most of the development effort is in the direction of applying digital computer logic and components in order to achieve reliability, lower cost, continuous visual display of the spectrum for monitoring and automatic digital recording of the memory content. The majority of modern designs employ pulse stretching with amplitude-to-time conversion in order to obtain 100 or more uniform channels which are free from interchannel boundary drift. This and many other aspects of the design of analysers are discussed in this second section of the book, which contains contributions from American and Canadian designers (C. J. Borkowski, G. C. Kelley, R. W. Schumann and F. S. Goulding) as well as from designers from laboratories in Great Britain (E. H. Cooke-Yarborough), France (J. Mey), Italy (E. Gatti) and Switzerland (D. Malder). It is well presented with a wealth of detail.

The later sections dealing with computer techniques, calibration and future trends are much shorter and deal with such techniques as analogue-to-digital conversion, storage, marginal testing, etc. Much of the information refers to analysers which are being developed at the present time, and so the opinions expressed are reasonably up to date, and the design data the latest available.

The book is one which can be thoroughly recommended to the specialist designer. Others, particularly the users of multichannel pulse height analysers, will find much of value in the book, but some of the later chapters dealing with the detailed circuit data may prove heavy going for such readers.

Denis Taylor

ECONOMICS OF ATOMIC POWER DEVELOPMENT IN INDIA AND THE INDIAN ATOMIC ENERGY PROGRAMME*

By Dr. H. J. BHABHA, F.R.S.

Long-range Need for Atomic Energy in India

THE coal reserves of India have been fairly well estimated. They may be taken at roughly 40,000 million tons, to which coking coal only contributes 2,780 million tons, while the rest comes from non-coking coal. Thus, the total reserves of coal in the ground amount roughly to a hundred tons per head of population. This is less than 1/20 of the per capita coal reserves of China, roughly 1/35 that of the United Kingdom, and about 1/150 that of the United States. Moreover, the per capita consumption of energy in the United States is equivalent to the burning of some 9 tons of coal per annum. The same per capita rate of consumption in India would correspond to the burning of a total of 3,600 million tons of coal per annum, and would therefore exhaust the coal reserves in about a decade. A doubling of the coal reserves would make scarcely any difference to the long-range picture.

The total hydroelectric potential of India is estimated at between 35 and 40 million kilowatts. The total hydroelectric potential, when fully harnessed, would therefore scarcely amount to 1/10 of a kilowatt of installed capacity per head of population. Much of this capacity is difficult and costly to harness. By comparison, the installed electrical capacity of the United States amounts to about 0·63 kilowatt per head, while it is 1·1 kilowatts per head in Norway. Another way of looking at the water-power resources is to note that an installed hydroelectric capacity of about 40 million kilowatts corresponds roughly to an annual consumption of about 120 million tons of coal, or barely a third of a ton per capita per annum. The water-power resources do not therefore materially alter the long-range energy-picture either.

The present oil production of India is very small. A considerable effort in finding new reserves of oil has been made recently, and will continue to be made for many years. These efforts have met with some success. It seems unlikely, however, that they will radically change the long-range energy-picture. One should remember that the world reserves of oil are a small fraction of its coal reserves.

We therefore come to the inescapable conclusion that the reserves of hydroelectric power and conventional fuels in India are insufficient to enable it to reach a high standard of living comparable even with the present standard of the industrially advanced countries.

The known Indian deposits of uranium ore containing more than 0·1 per cent uranium were until recently estimated to contain a total of some 15,000 tons of uranium. Much larger quantities of uranium are obtainable in ores of lower uranium content. A systematic survey for uranium in India was only begun in 1949, while surveys by helicopter and aeroplane fitted with scintillometers and by other modern techniques have only been undertaken since 1954. They have led to a number of new finds of radioactive minerals, and have already doubled the known reserves of uranium.

India has been known for several decades to have one of the largest deposits of monazite in the world, containing more than 9 per cent of thorium. It is estimated that these deposits on the south-west coast of India alone contain 150,000–180,000 tons of thorium in an easily extractable form. During the past six months the Raw Materials Division of the Department of Atomic Energy has made a spectacular new discovery of thorium- and uranium-containing minerals in the State of Bihar on the eastern side of India. This remarkable new deposit lies within ten feet of the surface and is estimated to contain more than 300,000 tons of thorium in a concentration of more than 10 per cent and more than 10,000 tons of uranium in a concentration of more than 0·35 per cent. Thus, the known reserves of uranium in ore containing more than 0·1 per cent amount to more than 30,000 tons, while the total reserves of thorium amount to about half a million tons. Assuming that breeding in power reactors will be possible eventually, as seems likely, the known Indian reserves of uranium and thorium become equivalent in energy value to more than thirty times its reserves of coal. Thus, the advent of atomic energy radically changes the long-range power-picture. The reserves of uranium and thorium are enough to support an annual per capita consumption of energy equal to that of the industrially most advanced countries for more than three centuries. We may confidently expect that, long before this, technology will have advanced to the stage of enabling us to obtain energy in a controlled manner from fusion rather than fission. The energy problem of the world will then have been solved for all practical purposes for ever.

Present Implications of Nuclear Power

I come now to the much more interesting questions concerning the relative economics of nuclear power in India to-day, and its bearing on the economy and planning during the next decade or two. In order to discuss this problem, we have to make some assumptions about the capital cost of atomic power stations and the cost of electricity generated by them.

We are at the very beginning of nuclear power generation. There are a large number of basically different types of reactors which may be used for the purpose. They may differ from each other in the form of the fuel, the particular moderator used, if any, and the system used for extracting heat. The fuel may be natural or enriched uranium or plutonium, used either as a metal or an oxide, or in the form of a ceramic, or in a solution. The moderator may be graphite or heavy water or beryllium oxide, or there may be no moderator at all as in a fast reactor. Finally, the heat may be extracted by circulating some gas, or by an organic fluid, or by a liquid metal;

* From an evening discourse given on September 5 during the Dublin meeting of the British Association.

or indeed the fuel itself, if in the form of a liquid, may be circulated for the extraction of heat.

Thus a very large number of combinations are possible leading to reactors of basically different design, each requiring the solution of special engineering problems. Even though many of these possibilities can be excluded after careful theoretical consideration, the number of possibilities that seem feasible on paper is still so large that several have not been tried at all, at least on a large scale. A number of different prototype power reactors are being built in the United States, and a number of them have been planned in the Soviet Union. None of these, except the pressurized water boiler, is at the stage to provide firm figures for an economic study. For most of the others we have only the vaguest ideas regarding cost. The United Kingdom has concentrated on the development of the graphite-moderated gas-cooled reactor. The firmest figures regarding cost are available for this type. Our present studies of the economics of atomic energy in India are therefore based mainly on this type of reactor, though in certain cases other types have also been considered.

The latest experience appears to show that the capital cost of a 60-megawatt station might be about £150 (Rs. 2,000) per kilowatt of net electrical capacity, of a 150-megawatt station between £120 (Rs. 1,600) and £130 (Rs. 1,730) per kilowatt, and of a station with a net electrical capacity of 250 megawatts per reactor perhaps £110 (Rs. 1,470) per kilowatt. We shall also assume in this discourse that power will be available at Rs. 0·044–0·05 (0·7–0·8 annas) per kilowatt hour, that is, between about 0·8 and 0·9*d*. per unit. It is also important to note that actual fuel cost only accounts for about one-third of this cost of power, the remaining two-thirds being capital charges and interest on fuel. These costs of power are based on taking capital charges at 13 per cent and a load factor of 80 per cent, corresponding to a utilization of 7,000 hours per annum.

Any plan for the utilization of an under-developed area must first ensure an adequate supply of power. An under-planning of the power requirements must be avoided in any event, since this would result in a throttling of the entire industrial development. It is preferable to err on the side of over-production of electric power, since the capital investment in plants for producing power is usually small compared with the capital investment in industries needed to consume the same amount of power.

In the present stage of development, atomic power stations are more likely to be competitive in power cost with conventional thermal stations the greater their size. Stations of 100–500 megawatts would have to be considered. The total power consumption in a small under-developed country is small, and even if the total consumption is considerable in a large under-developed country, this consumption may be so dispersed in a number of widely separated areas unconnected with each other as to be ineffective from the point of view of providing a large concentrated demand. Most under-developed areas of the world are either not covered by electric grids, or have such grids only in the neighbourhood of a few large cities. Thus, the fact that at present atomic power becomes competitive with conventional thermal power only in large stations tends to limit the scope of atomic power stations in most under-developed countries, since such large blocks of power as 300, or even 100, megawatts can only be utilized, in general, if fed into a grid.

All these general conclusions, however, are incorrect in the case of India. The total hydroelectric potential of India is not very large, and the seasonal nature of rainfall requires the construction of large dams, which usually take many years to build, and makes its harnessing relatively costly. It follows that in many parts of India power is generated from thermal energy, even though the power generated from it may be more costly. There are three important factors, the operation of which make nuclear power competitive in a major part of India. They are, first, the geographical distribution of the coalfields; secondly, the limited spare transport capacity available on the railways; and thirdly, the great shortage of power in certain industrial areas.

56 per cent of the total Indian coal reserves are located in the states of Bengal and Bihar, in the eastern corner of India. In 1955 about 80 per cent of the total production was in Bengal and Bihar, and all the coal for Delhi and Rajasthan in the north and west was supplied from these coalfields over a distance of roughly 1,500 miles. The supply to these two areas will still come from the same coalfields in 1961, although the total amount to be transported will increase by more than 50 per cent. A good part of the coal for the industrial areas of Ahmedabad and Madras is still supplied from Bengal and Bihar, and even when, at the end of the Second Five Year Plan in 1961, a substantial part comes to be supplied from the other coalfields in the centre and south of India, the distance over which coal will have to be hauled will still be of the order of 700 miles and more.

The present price of coal at the pit-heads varies from 15 to 21 Rs. per ton. The average tariff realized for transporting coal in 1955–56 on the Indian Railways was 2·85 hundredths of a rupee per ton per mile, while the average cost of carrying a ton of goods a mile for this period was 4·36 hundredths of a rupee, clearly showing that the present transport of coal on the Indian railways is subsidized. The present tariff for transporting a ton of coal over 500 miles is Rs. 14·25, over 700 miles Rs. 16·50 and over 1,500 miles Rs. 24·88, whereas the actual cost of transporting coal over these distances based on the average cost of haulage given above is Rs. 21·68, Rs. 30·52 and Rs. 65·04 respectively. The real cost of coal from the Bengal–Bihar collieries in Rajasthan and Delhi is therefore more than Rs. 80 per ton, as is its real cost to-day in Ahmedabad and Madras also. Even when coal comes to be supplied to the industrial areas of Ahmedabad, Bombay and Madras from the Central India coalfields at a distance of more than 700 miles, the real cost of this coal will be about Rs. 50 per ton.

It is estimated that the cost of electricity from a thermal power station would be about 4·7 hundredths of a rupee, or 0·85*d*. per unit, with a total cost of Rs. 50 or £3·75 per ton. We should, therefore, expect power from atomic power stations to be competitive with power from thermal power stations in areas remote from the coalfields such as Ahmedabad, Bombay, Delhi and Madras.

In planning for the future, we must also bear in mind the direction in which costs may be expected to move. Coal prices, which are controlled, have risen by more than 50 per cent during the past twelve years. On the other hand, atomic power may be expected to become progressively cheaper as a result of technical advances resulting in lower capital costs,

higher temperatures of operation, and higher efficiencies. There is little doubt that during the next ten years nuclear power from improved versions of the graphite-moderated gas-cooled reactors will be cheaper than thermal power at most places in India remote from the coalfields.

I consider next the second factor already mentioned, namely, the effect of the transport of coal on the railway system and the economy as a whole. The average tariffs for carrying 1 ton of coal and other goods over 1 mile is given in Table 1.

Table 1. Freight Charge per Ton Mile on the Railways

	Rs./100
Coal on public railways	2·85
Coal on non-government railways	5·47
Grains	5·36
Oilseeds	6·72
Other commodities	6·67
Actual average cost of haulage (broad gauge)	4·36

On the other hand, the actual cost of hauling a ton of goods a mile, taking interest on the total present capital invested in the railways at 4 per cent per annum, works out at 4·36 hundredths of a rupee. This clearly shows that the transport of coal is subsidized in the wider interest of the economy as a whole.

Under-planning of power appears to have been a feature of the Indian economy during the past decade. This shortage of power results in a remarkably high load factor for the grid systems as a whole. The average load factor for the Ahmedabad grid is 63 per cent, and that for the Bombay grid 69 per cent. Even on a conservative basis, therefore, it would appear to be quite feasible to have an atomic power station of a suitable size, say, of 150 megawatts and capable of being doubled later by the addition of a second reactor, in any of the areas I have mentioned, and operated on a very high load factor, keeping the present thermal stations for peak loads and as stand-bys.

Relative Economics of an Atomic and a Coal-fired Power Station

It is instructive to consider a particular example in greater detail, and I take for this purpose the relative economics of an atomic and coal-fired power station of 150 megawatts located not far from Ahmedabad. The cost of coal at the station, even if it were brought from the nearest coalfields in Central India, would be nearly Rs. 50 per ton, if its transport were not subsidized. At this price for coal the real price of electricity would be 4·7 hundredths of a rupee (0·85*d.*) per unit, with capital charges at 13 per cent. The real price of coal may actually be higher because of loss of coal in handling and due to pilferage in transit.

The capital cost of an atomic power station of 150 megawatts might be taken roundly at Rs. 25 crores (£18·75 million), while the cost of a coal-fired station may be taken at Rs. 15 crores (£11·25 million). Thus the atomic station will cost Rs. 10 crores (£7·5 million) more in capital investment. To this must be added the investment in uranium, which may be taken at another Rs. 5·6 crores or £4 million. The total difference in capital required is therefore about Rs. 15 crores or £11·25 million. This, however, is not the whole story, and we have to look further into the relative costs of the two to the economy as a whole.

A coal-fired station would require about 1,300 tons of coal per day, assuming that a pound of coal is required for the generation of a unit of electricity. The station would therefore consume more than 450,000 tons of coal per annum, the transport of which over a distance of 700 miles would mean a permanent locking up of 1,200 wagons and nearly 20 locomotives, representing a capital investment of Rs. 2·2 crores or more than £1·6 million. The transport of this coal would utilize on the railways 300 million ton miles per annum of carrying capacity. We have to make some estimate for the saving which would result to the economy as a whole, if this transport of coal were saved by replacing a coal-fired by an atomic power station. There are two ways of doing this calculation. Since the average cost of a mile of railway track is Rs. 550,000, (£41,000), while the maximum carrying capacity of a mile of single track is 6·1 million ton miles per annum, one could charge roughly Rs. 100,000 (£7,500) as the capital investment on railway track for a carrying capacity of one million ton-miles of goods per annum. The capital chargeable on account of track for the above coal transport therefore amounts to roughly Rs. 3 crores or another £2·2 million. Another way of looking at the matter is to calculate the increased earnings of the railways, which would result if the same carrying capacity were used for the transport of other goods instead of in carrying coal. These would be in two parts: first, the saving in subsidy on the transport of coal, and secondly, the additional revenue accruing to the railways on diverting this capacity to the transport of other commodities. The saving in subsidy amounts to Rs. 0·63 crores. The weighted average of revenue for carrying grains, oil and other commodities is 6·54 hundredths of a rupee per ton mile for the year 1955–56. As the average cost of carrying goods per ton mile is only 4·36 hundredths of a rupee, the net revenue to the railways under this head would be Rs. 0·65 crores. So the total increase in the earnings would amount to Rs. 1·28 crores or £960,000 per annum. If one assumes that the increase in railway capacity would have to be undertaken in any event for development purposes, the increased earnings on the railways, due to the substitution of the coal traffic required for a coal-fired station by general goods traffic, can be regarded as interest on the extra capital investment required by an atomic power station, which we have seen to be about Rs. 15 crores or £11 million. This would therefore represent a return on capital of nearly 8·5 per cent over and above the interest on capital at 5 per cent, which is already included in the cost of power from an atomic power station.

In calculating the relative costs of atomic and coal power to the economy as a whole, we have to carry the analysis further and work out the relative capital investment required to produce the 50 tons of uranium per annum needed by the atomic power station or the 450,000 tons of coal required by the coal-fired station. At 50 per cent overall recovery and assuming a pessimistically low-grade ore containing 0·05 per cent uranium, some 200,000 tons of ore must be mined. Table 2 gives the relative capital investment required for mining an additional million tons per annum of coal and of washing it, compared with the capital investment required for mining the equivalent amount of uranium ore, of extracting the uranium from the ore, of purifying it, and fabricating it into fuel elements.

Table 2. RELATIVE CAPITAL INVESTMENTS IN PRODUCING 1 MILLION TONS OF COAL OR 110* TONS OF URANIUM (RS. IN CRORES)

	Coal	Uranium
Mining	3·5	1·5
Washeries	1·2	
Uranium processing and fabricating facilities		3·5
	4·7	5·0

Note: An overall recovery of only 50 per cent assumed in the uranium plant, requiring about 450,000 tons of 0·05 per cent ore to be mined.

* The Railway Fuel Economy Inquiry Committee, 1953, estimates that for coal consumed by the Indian Railways the loss in handling and due to pilferage in transit is 7 per cent. This would reduce the equivalent quantity of uranium from 110 tons to about 100 tons, and the total at the bottom of the second column to 4·65.

Table 2 shows again that the capital investment in the additional annual production of coal is comparable with the capital investment in the additional production of uranium. It would be substantially more with a richer uranium ore.

The example just given is typical of the situation which we find in many important industrial centres in India, which are remote from the coalfields, such as Delhi, Bombay, and Madras.

Utilization of Thorium

It has been mentioned that the total reserves of thorium in India amount to more than 500,000 tons in a readily extractable form, while the total known reserves of uranium are less than a tenth of this. The aim of a long-range atomic-power programme in India must, therefore, be to base the generation of nuclear power as soon as possible on thorium rather than uranium. Once concentrated fuel in the form of uranium-235, or uranium-233, or plutonium, is available, it should be possible to generate power in breeder reactors which breed more fissionable material, uranium-233 or plutonium, in the source materials thorium and natural uranium, than they burn. The reactor at Dounreay is a large-scale experiment in this direction, and if it succeeds in breeding, and at the same time is shown to be safe and easy to control, it should open up a new chapter in the generation of atomic power. There are other possibilities of breeding, as, for example, with reactors moderated with heavy water. Since all power reactors intended for breeding appear to require the use of enriched or pure fissionable material, a self-sufficient programme must provide for the production of such material.

So far as India is concerned, we consider isotope separation plants for the production of uranium-235 by the presently known methods out of the question, due to their high cost, and even more because of their enormous consumption of electric power. The best way of obtaining fissionable material appears to be to produce plutonium as a by-product in atomic power stations working on natural uranium. A simple calculation shows that a million kilowatts of installed electrical capacity in nuclear power plants would yield approximately 900 kilograms of plutonium per annum. This could be used to fuel the second stage of atomic power stations intended to breed, and which could therefore be fed thereafter only with thorium. The plutonium produced in the natural uranium nuclear power plants would therefore be used to instal new electrical capacity each year. The amount of new electrical capacity which could be started off annually, to be fuelled from the plutonium produced in natural uranium reactors having a million kilowatts of electrical capacity, would depend on several questions, the answers to which are not known or not known sufficiently accurately. One must await the results of the experiments which are being done in the United Kingdom, the United States, and the U.S.S.R., on large-scale experimental power plants, before reasonably accurate planning is possible. The Department of Atomic Energy in India is at present engaged in working out various possible power programmes with different assumptions regarding the data required.

It seems likely that breeder power stations may begin to operate by about 1965. In order that enough plutonium should be available at that time for fuelling such stations, it is clearly necessary to start on an atomic power programme based on natural uranium reactors very soon. If the construction of such reactors were to be taken up next year, they would only begin to operate in 1962, and plutonium would therefore only become available in quantity by 1965.

The Indian Atomic Energy Programme

I will conclude by describing briefly the work that is being done in India to develop atomic energy as a source of electric power and to promote its use in agriculture, biology, and medicine. On the industrial side, we intend to produce all the materials required for a full atomic power programme. For this reason, we started by setting up a plant at Alwaye in south India to treat the well-known monazite sands on the west coast. In addition to producing rare earths and trisodium phosphate (a cleaning material sold in the market), this plant produces a cake containing thorium and uranium. This cake is brought to the plant at Trombay near Bombay, which produces a very pure thorium salt and also a uranium salt. It was built by Indian scientists and engineers and has been in operation since 1954. Its capacity was increased six-fold last year.

We have designed a small uranium plant which will turn this uranium salt into reactor-grade uranium metal, and we expect to have this plant in operation by the middle of 1958. This plant will give us enough uranium metal for experimental purposes and for use in the reactors that are under construction at present. It will also give our scientific and technical staff the necessary experience for the design and construction of the large uranium plants which will be required by a full atomic power programme.

A small plant for the fabrication of fuel elements has also been designed, and its construction is being undertaken forthwith. Besides producing the fuel elements for our present natural uranium reactors, it will also enable research and development work to be carried out on new types of fuel elements and their canning.

India is one of the largest producers in the world of the rare mineral beryl from which the metal beryllium can be obtained, the present annual production being several thousand tons of high-grade beryl. Beryllium oxide may have interesting possibilities as a moderator, and the metal or one of its alloys holds out great promise as a canning material. A large pilot-plant for producing atomically pure beryllium oxide of nuclear purity and sintering it into bricks is also being designed. Its capacity will be about 15 tons of beryllium oxide per annum, but it will be capable of expansion to several times this size. Preliminary studies indicate that the cost of beryllium oxide produced in this plant will be lower

than the cost at which it is being produced in Europe at present.

We also intend to produce heavy water in quantity, and the decision was taken two years ago to produce heavy water and fertilizer together in a large plant which is being built at Nangal in the north. This plant will produce more than 340,000 tons of nitrogenous fertilizer annually, and between 10 and 20 tons of heavy water. Hydrogen for the ammonia plant will be made electrolytically. The heavy hydrogen will be concentrated in the last stage in the electrolysis cells, which will be arranged in cascade. The heavy hydrogen from these cells, which will comprise between 20 and 40 per cent of the total stream, will be liquefied and the deuterium extracted by the hydrogen distillation process. The plant has been placed at Nangal, so that it can draw cheap power from the dam at Bhakra. It will consume 160,000 kilowatts of electric power, and cheapness of power is essential for the economics of the process. It is estimated that by charging to heavy water only the direct costs involved in its production, the cost of heavy water will be about 20 dollars per lb., which is substantially lower than the present world price. Production will commence in 1960. Several other large fertilizer plants are expected to be constructed during the Second Five Year Plan, and it is the intention of the Government to produce heavy water in all of them.

We are also studying the erection of a plant to make atomically pure graphite from the coke produced in a refinery in Assam. Experiments which are under way at the Atomic Energy Establishment at Trombay have already shown that graphite of a high density can be produced by a method which is being tried.

Zirconium is another metal which has promise as a canning material. In order that it should be so used, hafnium has at first to be separated from it and a good deal of research work has been done on the separation of hafnium from zirconium. A process is now being tried out which is even more promising than the one reported by us at the Geneva Conference on the Peaceful Uses of Atomic Energy. This method promises to yield metallic zirconium free from hafnium in one step. Zircon, the mineral from which zirconium can be obtained, is found as a constituent of the famous beach sands on the south-west coast of India and is available in plentiful supply.

Any country which does not wish to depend wholly upon outside aid must have its own research and development organization, not only for investigating the many possibilities which remain unexplored, but also because, even in fields where general knowledge is available, practical experience must be obtained. The Atomic Energy Establishment at Trombay, near Bombay, which was formally inaugurated by the Prime Minister in January this year, is India's centre for research and development in the field of atomic energy.

A layout of the entire Establishment has been prepared, and some buildings completed, while the construction of others will start very soon. Some of the new laboratories will be ready early next year, although all the buildings planned at present will not be ready until 1959. The Establishment is located at Trombay, some fifteen miles from the centre of Bombay. The site of the Establishment, which covers an area of more than 2,000 acres, is completely separated from the rest of the industrial area of Trombay by Trombay Hill on its west. Its eastern side lies on the upper reaches of Bombay Harbour.

We did not wait for the new buildings before starting the research activities of the Establishment. The Physics and Engineering Divisions were located in the Tata Institute of Fundamental Research at the old Yacht Club building, and in war-time hutments on its new site at Colaba. A warehouse in another part of Bombay was converted for housing the Chemistry Division, while the Biological and Medical Divisions were set up at the Indian Cancer Research Centre. The total scientific and technical staff of the Establishment is now about three hundred, and it will increase to more than eight hundred by 1959. By that time the total number of workers on the site, including administrative, maintenance and workshop staff, will be more than two thousand.

To ensure a steady supply of trained scientific and technical personnel, we have started a training programme under which 250 young graduates and engineers will be recruited annually from the universities and given supplementary training for a year to fit them for work in our atomic energy programme. The first course commenced in August this year with 170 trainees. It is hoped to increase the intake of this school to 350 a year in due course.

APSARA, India's first atomic reactor, of the swimming pool type, became critical for the first time on August 4, 1956. It is the first reactor to go into operation in Asia, outside the U.S.S.R. It was designed, engineered, and built entirely by our own people and by Indian industry, except for the fuel elements. The fuel elements, which contain enriched uranium, have been provided by the United Kingdom Atomic Energy Authority.

The decision to build this reactor was taken in April 1955. A firm decision on the basic design was made in August 1955, and it took about one year to complete its construction.

As soon as the decision to build the swimming pool reactor was taken in early 1955, we turned to the next step of building a powerful high-flux reactor for engineering research. We were considering several different types, when we received a generous offer from the Canadian Government to set up a reactor of the *NRX* type in India. The decision to proceed with the joint project was taken in August 1955, and the ground for it was broken in February 1956. We expect this reactor to be completed by the end of 1958. This reactor requires some 20 tons of heavy water, which was sold to us by the United States Atomic Energy Commission.

A short while ago, we decided to build a third, zero-energy, reactor, which will enable us to study the effect of different lattices, shapes and sizes of fuel elements, mixed lattices containing uranium or plutonium and thorium, and so on. We expect to have this reactor in operation in 1958 also, and indeed, it may be the second reactor actually to go into operation in India.

The immediate need in many parts of India is for small power stations of 20–50 megawatts, and it is our intention to study for this purpose reactors moderated with beryllium oxide, gas-cooled, and working on natural or slightly enriched uranium. The critical size of beryllium-moderated reactors is smaller than graphite-moderated reactors, and preliminary calculations show that they may well be more economical in the power-range below about 20 megawatts. For this purpose, we have had for

some years a joint project with the Commissariat à l'Énergie Atomique for studying the properties of beryllium oxide as a moderator. A small group at our Trombay Establishment is now actively engaged in feasibility studies on reactors moderated with beryllium oxide of a power output of less than 30 megawatts.

The Indian atomic energy programme is of a very modest size, compared with the programmes in the United States, the Soviet Union, and the United Kingdom. It has no military component and I cannot but recall on this occasion the words of the Prime Minister, Mr. Nehru, at the inauguration of the Trombay Establishment, when he said "whatever might happen, whatever the circumstances, we shall never use atomic energy for evil purposes". Although the Atomic Energy Commission was established as an advisory body in 1948 in the Ministry of Natural Resources and Scientific Research, no important effort to develop this work was made until a separate department of the Government of India with the full powers of a ministry was established in August 1954. Since then the work has developed very rapidly and the expenditure on atomic energy has grown about thirteen-fold within three years. Only a modest beginning has been made, but one that holds out promise of important developments, which may well help to accelerate the industrialization of India.

OPTICAL DEFINITION OF THE METRE

By Dr. H. BARRELL

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A RECOMMENDATION to define the metre in terms of light waves has recently been made by the Comité Consultatif pour la Définition du Mètre, one of the five advisory committees of the Comité International des Poids et Mesures which periodically meet to give expert consideration and make recommendations relating to units and standards of measurement; the other four are concerned with temperature, electricity, photometry and the definition of the second of time, respectively. The suggestion to use the wave-length of light as a natural standard of length, first propounded by J. Babinet[1] in 1829 during the period when the wave theory of light was being formulated and established, has thus at long last led to the following conclusion: that the metre be defined as equal to 1 650 763·73 times the wave-length *in vacuo* of the orange-red radiation corresponding to the transition between the energy-levels $2p_{10}$ and $5d_5$ of the krypton-86 atom.

The first public announcement about this important development has just been made by the National Research Council of Canada; Dr. L. E. Howlett, director of the Division of Applied Physics of the National Research Council, is chairman of the Comité Consultatif and also the member for Canada on the Comité International, which will consider the recommendation during its session in 1958. If accepted, as appears likely, the wave-length definition will then be submitted for the approval of the Conférence Générale des Poids et Mesures (the supreme authority in the international metric organization) when it next assembles in 1960. Adoption would mean that the metre depended once again upon a natural standard—a conception which greatly attracted the creators of the metric system during the last decade of the eighteenth century. But the earlier definition was based, as is well known, on a terrestrial dimension which was afterwards found to be rather inconvenient as the means of reference, so it became superseded by one expressed in terms of an arbitrary material standard—the Mètre des Archives, a platinum end-standard—originally constructed to serve merely as a convenient working standard representing a ten-millionth part of the length of a certain polar quadrant of the Earth. The Mètre des Archives was superseded in 1889 by the International Prototype Metre—a platinum–iridium line-standard—which, with its authorized copies, constitutes the present means of maintaining the metric unit of length throughout the world.

The Comité Consultatif pour la Définition du Mètre was established in 1952 as the result of a resolution[2], adopted by the Conférence Générale in 1948, which directed attention to the importance, for the practical definition and measurement of length, of advances made in the production of high-quality monochromatic light from pure isotopes (mononuclides) of even atomic charge and mass (zero nuclear spin). The advisory committee, which comprises representatives from the several national standards laboratories and the Bureau International des Poids et Mesures, as well as independent experts in spectroscopy and interferometry, held its first meetings in 1953. Recommendations[3] were then made which (*a*) strongly favoured the wave-length of a radiation from a mononuclide propagated *in vacuo* as the means of re-defining the metre, (*b*) proposed that the radiation be specified solely by the two spectroscopic terms denoting the atomic states between which the energy transition takes place, and (*c*) described the modalities of transfer from the material to the natural standard. The committee found itself unable at that date to select the source and radiation best suited to serve as the ultimate standard owing to the lack of sufficient comparable experimental observations on the radiations from mononuclides. Continuity with the existing definition of the metre unit was to be preserved through the intermediary of the relationship $\lambda_R = 6438{\cdot}4696 \times 10^{-10}$ m., derived from nine independent measurements[4] of the metre in terms of the wave-length λ_R of the red line of cadmium in standard air, that is, dry air at 15° C. under standard atmospheric pressure (1 013 250 dynes/cm.^{2}) and containing 0·03 per cent by volume of carbon dioxide. Since any new wave-length standard was to be related to the vacuum condition, it was necessary to specify a dispersion formula for standard air and, to this end, the committee adopted that evaluated by B. Edlén[5]. These provisions ensure that, so far as

possible, the numerical values of all optical wavelengths expressed in angstroms will remain unchanged and that 1 A. becomes, by definition, equal to 10^{-10} m. exactly. It may be recalled that the value λ_R = 6438·4696 A. was adopted[4] as the spectroscopic reference standard in 1907 and thereby became the means of defining the international angstrom—the unit that has since served for all spectroscopic measurements of wave-length; also that the Conférence Générale of 1927 gave formal sanction[5], as an interim procedure, to measurements of length on the basis of 1 m. = 1 553 164·13 λ_R (corresponding to λ_R = 6438·4696 × 10^{-10} m.) as an alternative to direct reference to the Prototype Metre or its copies.

The recommendations made at the 1953 meetings of the advisory committee were communicated to the Conférence Générale in 1954[6], and, following this, many investigations were initiated on the spectroscopic qualities and wave-lengths of radiations emitted by the mononuclides cadmium-114, krypton-84, krypton-86 and mercury-198. The results of these investigations, which were carried out at the Bureau International des Poids et Mesures and the standards laboratories of Australia, Canada, Germany, Japan, the United Kingdom, the United States and the U.S.S.R., were discussed at the meeting of the Comité Consultatif held last September at the Bureau, and the recommendation for an optical definition of the metre in the terms already quoted was unanimously accepted.

The limit of interference of the recommended radiation of krypton-86 is of the order of 0·8 m. when excited from the hot-cathode discharge lamp[9] perfected by E. Engelhard for operation when cooled to the triple point of nitrogen (63° K.). With such a source, the effects of small departures from the ideal conditions of excitation implied by the committee's specification of atomic states are calculable. The isotope of krypton of mass 86 was selected as the source, rather than that of mass 84, because the former is easier to isolate by the process of thermal diffusion used for separating the constituents of natural krypton. It is estimated by the Comité Consultatif that the reproducibility of the recommended new definition of the metre is within the range of 1–3 parts in 10^9. This figure of merit is given for comparison with that of 2–3 parts in 10^7, which is generally accepted to be the reproducibility of the present definition of the metre in terms of the material standards.

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STRUCTURE AND FUNCTIONING OF THE NERVOUS SYSTEM

IN his presidential address to Section D (Zoology) of the British Association, meeting at Dublin on September 5, Prof. J. Z. Young considered the problem of describing the self-adapting control systems of living organisms and the development of memories within the nervous system. He referred to an organism as a communication system handling signals in various codes, two examples of which are the chemical signals of the endocrine system and the impulse signals of the nervous system. The storage of memories within the nervous system is regarded as a special case of a more general principle, whereby coded representations of events in the environment are stored in readiness to control the selection of those responses which had survival value in the past. This concept was illustrated by reference to the selective activation of groups of neurones in the movement-control centres of the nervous system during the behavioural responses of an animal. Electrical stimulation of such centres in appropriate areas of the octopus brain can release elaborate patterns of action, such as walking or swimming, but little is known about how the connexions between the neurones of these centres evoke the patterns, how it is ensured that actions are performed in a steady and well-regulated manner or how the appropriate actions are selected in normal life on the basis of information stored in the memory or received from the sense organs.

The first paper of the symposium following the presidential address, which was presented by Dr. W. K. Taylor, attempted to show how some of these functional characteristics of the nervous system are also possessed by certain types of electrical network formed by interconnecting electronic analogues of neurones. Each analogue unit was designed to simulate what are believed to be the important features of the electrical activity of neurones, so far as the transmission and transformation of the signals that convey information throughout the nervous system are concerned. The assembly of units constitutes an analogue computer, since it can be employed for investigating the electrical activity of any network believed to have functional significance by making appropriate inter-connexions between the units.

Before the units could be designed it was necessary to consider the code of signals used by the nervous system, and it was concluded that most of the physiological evidence supports the theory that the code is effectively a special form of frequency modulation in which the carrier frequency can be modulated down to zero frequency or up to a maximum of several hundred cycles per second. This analogy was illustrated by reference to a method of demodulating a frequency-modulated wave, in which each cycle is replaced by a pulse of any constant shape that could, in particular, be the same shape as the nerve-action potential. The modulating signal is

recovered by passing the pulses through a low-pass filter, and the analogy is strengthened by the fact that nerve impulses are always smoothed by what are effectively low-pass filters whenever they are used for controlling movements. The similarity between waveforms of the tension developed by a single motor unit and the output of a low-pass filter in response to a train of impulses served to illustrate this point. It was suggested that neurones can be regarded as frequency-modulating devices in which a stimulus is converted into a modulating signal that controls the rate at which nerve impulses are generated. Changes in membrane potential of crustacean stretch-receptor cells recorded by Eyzaguirre and Kuffler (1955) were shown to support this analogy if the depolarization due to stretch is identified with the modulating signal. Adaptation of neurones can be thought of as a decrease in the modulating signal for a constant stimulus and hence separated from the modulation process. The changes in membrane potential referred to above support this view, since the 'firing level' of depolarization remains almost constant during adaptation to a constant stretch, whereas the rate of depolarization following each impulse gradually decreases.

A low-pass electrical filter has also been designed to simulate the transformation from nerve-action potential to post-synaptic potential that occurs when a nerve impulse travelling along the axon of one neurone arrives at a second neurone and either tends to increase or decrease its firing frequency. The behaviour of the electrical analogues is consistent with the hypothesis that the firing frequency of a neurone would be modulated by the resultant post-synaptic potential produced by the algebraic summation of all the changes in synaptic current produced by impulses arriving at all the synaptic endings. Indirect evidence in favour of the hypothesis is to be found in the form of Kolmodin's recordings from single interneurones in the spinal cord of the cat, the firing frequency of which can be increased or decreased in a controlled manner by appropriate natural stimulation of the skin or of muscle-stretch receptors.

The frequency modulation analogy was also illustrated by showing that four sets of frequency-modulated impulses within the physiological range of frequencies will communicate sufficient information to control intelligible speech. Recordings of four sets of frequency-modulated pulses generated by four neurone analogue units sounded like variable-frequency nerve-action-potential recordings, but when the same pulses were passed through a demodulator possessing similar transfer characteristics to muscle and used to control a speech synthesizer, the words "British Association" were formed. This result could not have been obtained with the specified form of demodulator if any code other than the frequency modulation of the constant-area pulses had been employed.

The hypothesis that information storage or memory resides in changes in synaptic potency was considered as the basis of at least a large proportion of the observed learning behaviour of animals. When changes in synaptic potency were simulated in the analogue computer it became possible to investigate neural theories of learning. An example of this was described, in which the computer was set up to simulate a neuronal network that was thought to be capable of learning to recognize shapes. The input apparatus took the form of a model eye that could follow moving shapes and generate signals corresponding to the light intensity distribution over the receptive field. The set of outputs from the 'eye' supplied inputs to the neuronal network, and additional inputs were derived from sound receptors sensitive to different tones. For each input tone there was a corresponding output tone under the control of the network under investigation, but visual inputs initially had no power to produce output sounds. 'Training' was then commenced by presenting shapes, such as letters of the alphabet, at the same time sounding an input tone, arbitrarily selected from a range of tones. If the training was successful the output eventually responded by giving the tone that had previously been associated with a particular shape when the shape was presented without sounding its 'name' in the tone-language. The learning powers of the network could thus be investigated experimentally. An example of how one particular network responded to distorted forms of the letters *T* and *L*, after being trained to respond correctly to standard forms of the letters, was illustrated by slides showing the distorted letters and the output responses. A number of networks had been found to possess this ability to learn the 'names' of shapes, and all had certain features in common. While this could not be taken as evidence that the nervous system contains similar networks, it provided concrete hypotheses that could in principle be tested and which served as a guide to further research.

In a paper entitled "The Analysis of Nerve Function", Dr. J. W. S. Pringle suggested that knowledge of the physiology of the nervous system should be the zoologist's starting point for what he must always regard as his main objective—an understanding of the activities and working of the animal as a whole in its normal relationship to the environment. He described the function of the nervous system as that of providing the animal with its means of rapid adaptation, and advocated the use of information-flow diagrams as a convenient method of illustrating different types of nerve function. An example of a simple information-flow diagram was given in which information flowing from the eye to the brain and back to the eye muscles is represented by a single directed line, thus illustrating the principle of eye-movement control without confusing the picture by attempting to represent the internal structure which has so far proved too complicated for complete description.

Two indirect methods that can be applied to the problem of correlating structure and functioning were suggested. The first is to look for simple structures in which the integrative action could be analysed in some detail, reasoning from these to more complex systems. The second involves a broad survey of the organization of nervous systems in as wide a variety of animals as possible, a search for principles or organization derived from the study of man-made automata and an assessment of the extent to which the organization of the nervous system could be understood in terms of these principles.

The study of the cardiac ganglion of the decapod Crustacea provides an example of the first method. There are only nine neurones in this ganglion, and the interconnexions produce the interactions that result in the generation of a complex rhythmic pattern of activity. Maynard has found that only continuous steady responses are obtained if the interaction is

reduced, so that it is necessary to consider the ganglion as a unit. In normal operation, the order in which the bursts of impulses are generated is repeated with regularity and the number of impulses in the bursts is nearly constant. This suggests that the neurone and synapse characteristics are very stable and that the noise-level is very low. As a second example, Dr. Pringle referred to his own studies of the more complicated and less understood nervous mechanisms responsible for the cicada song. As in the case of the cardiac ganglion, only part of the nervous system is involved and there is no evidence of learning. The form of the generated patterns is innate and genetically controlled.

In order to gain some insight into how the property of memory may be achieved in the higher centres of the nervous systems of animals Dr. Pringle investigated the second method. He referred to control systems in which the order of past events is re-recorded and used for predicting future sequences by a process analogous to the trial and error learning of animals.

The investigation of relatively simple nervous systems containing a comparatively small number of neurones was also the subject of papers by Dr. H. P. Whiting and Dr. D. M. Vowles. Dr. Whiting described the distinctive features in the organization of the several hundred large neurones in the brain and spinal cord of embryonic and laval lampreys. In the brain, for example, more than a dozen pairs of neurones are distinct in position and in nervous connexions. At hatching several of the brain cells are large and distinctive. There are several pairs of Müller nerve cells, increasing to ten distinct pairs in the adult, and it was suggested that each has a particular co-ordinating function in linking the sensory system of the head with the swimming system of the trunk. One pair of Mauthner nerve cells, each with a long process descending to the opposite side of the spinal cord, has a function related to the maintenance of equilibrium. Other distinct pairs of neurones with shorter processes which do not extend into the spinal cord were also to be seen in the brain of the newly hatched animal, and these were thought to represent tract systems of the adult brain, one cell doing what will be the work of many in the adult. Before the animal hatches, sensory (Rohon–Beard cells), motor (primary motor somatic cells), and two types of internuncial cells, which repeat at regular intervals and which link with the motor system, can be identified in the spinal cord. These four types are comparatively large; they have a definite position in the cord and a specific form. A similar regularity in the cord is very marked in trout embryos. The nerve cells are at first irregular in shape and position; then, as the earliest to develop form their synaptic connexions, so the cell body of each moves into a definite position in the spinal cord pattern and acquires a fairly specific shape and connexions. This can be seen in the sensory and motor cells and also in three pairs of co-ordinatory cells which lie at the level of the pectoral fins. Dr. Whiting thought that the paired arrangement of the large nerve cells in primitive vertebrates may also be found when smaller cells are examined. He reached the tentative conclusion that, during the evolution of vertebrates, nerve cells have become smaller and much more numerous relative to the size of the animal: at the same time the connexions established by nerve cells have become more labile, and the behaviour of the animal is determined more by what is going on in a local population of nerve cells than by the function of any single cell. An evolution in this direction fans out on a much wider scale in the mammalian cortex.

The fact that there is less information to deal with when one considers a relatively simple nervous system, and hence a greater possibility of describing the interactions within the system was emphasized by Dr. Vowles in his paper on the structure and function of insect nervous systems. Giant fibres give rapid conduction and enable insects to respond quickly, but the large size reduces the number of fibres and hence the range of possible responses.

Although the number of neurones in the ganglia of insect nervous systems was relatively small, some of the complex functions that could be performed resembled corresponding functions in vertebrates. The discrimination of flowers by flicker employed by bees was quoted as an example of the wastage of information that occurs between the receptors and effectors of insects. This is inevitable since the eye collects more information than the motor system can handle. The wastage is thought to be much less with mammals. As in the larval lamprey, the neurones of the insect nervous system are found to form regular patterns as development proceeds, the order of cell division being muscle first, followed by motor and finally sensory cells.

The final paper of the symposium, by Dr. M. J. Wells, described a study of the processes involved in the learning of touch discrimination in the octopus. The octopus is peculiarly suitable because of the considerable structural separation of the parts concerned with sensory integrative and motor processes. Experiments suggest that the animals are unable to distinguish the shape of objects but that differences in texture can be detected. It is thought that the inability to discriminate shapes is a consequence of the extreme flexibility of the arms of the octopus, and that we learn to distinguish shapes by making use of information from muscles and joint receptors in addition to the information from touch receptors.

The absence of joints in the octopus is considered to be equivalent to a practically infinite number of bending places, and it seems improbable that the animal can have a sensory apparatus of the complexity necessary to define the relative position of its armtips or suckers with any accuracy. Octopus appears to learn to recognize objects from the characteristic frequencies of nerve impulses that different surface textures produce in the nerves coming from the arms. Dr. Wells compared the tactile learning before and after removal of the optic lobes and found no change, whereas damage to the considerably smaller volume of the vertical lobe results in the animal requiring more trials to attain a given standard of response. Extensive damage to the inferior frontal-subfrontal lobe system results in destruction of the octopus's ability to learn to discriminate between objects by touch, but has no effect on movements or on visual learning. It was concluded that the inferior frontal-subfrontal system is exclusively concerned with the integration of surface tactile information. The apparent limitation to frequency discrimination within this system was considered to be favourable from the point of view of the study of learning processes and the structures associated with them.

W. K. Taylor

OBITUARY

Prof. Heinrich Balss

THE German zoologist Heinrich Balss, for many years chief conservator of the Zoologische Staatssammlung, Munich, died at Planegg on September 17, aged seventy-one. He was a well-known specialist on the higher Crustacea and contributed the sections on decapods and stomatopods to Kükenthal and Krumbach's "Handbuch der Zoologie" and also to Bronn's "Klassen und Ordnungen des Tierreichs".

Balss received his early education at Mainz, where he was born on June 3, 1886. After a semester at Heidelberg (1904) he transferred to Munich, with which University and city he was associated for the rest of his life—with a break during the First World War. On obtaining his doctorate in natural science, he was appointed assistant to Prof. R. von Hertwig; he became conservator in 1918, chief conservator about 1928 and received the title of professor in 1925. In September 1937, because he was of Jewish extraction on his mother's side, he was retired on half pay though allowed the use of his room at the Staatssammlung. He was re-instated after the fall of the Hitler régime and retired voluntarily in 1951.

In his formative years Balss owed much to the inspiration of Franz Doflein, with whom he collaborated in studying material of the Hamburg Magellan and German Deep-Sea Expeditions (1912 and 1913). Doflein's rich collection from Japanese waters formed the basis of a series of papers by Balss on "Ostasiasische Decapoden I–V" (1913–14 and 1922–24). Reports by him appear in the results of numerous German expeditions, and many other countries sent him material for determination and description. He was the ideal systematist—painstaking, methodical and thorough in everything that he undertook. He did much to elucidate the classification of the large and difficult group of spider-crabs and of the even more difficult Xanthidae—a family of nearly a thousand species. The body of work which he produced between 1910 and 1938 testifies to his industry and ability, and he has left a permanent mark on the literature of his subject.

With the publication of the "Handbuch" in 1927 Balss became known to a much wider public, and the new Bronn's "Tierreich" will greatly enhance his reputation. It is a larger and more comprehensive work and, during his enforced retirement, Balss was able to devote his full time to it. The part on the Stomatopoda appeared in 1938. He undertook the whole of the volume on Decapoda, ontogeny and physiology excepted, and the manuscript was finished about 1940. Seven parts, five by Balss, were published between 1940 and 1945; then, owing to difficult post-war conditions, only two parts appeared during the next nine years. Meanwhile, the author's health was impaired by a serious illness, and these delays were most disappointing. The systematic part (12) was published last summer during his final illness; he was able to bring it more or less up to date, especially as regards the Caridea, and it includes a very high proportion of the known genera, fossil as well as recent. It is to be hoped that the sections on zoogeography, palæontology and phylogeny and the bibliography will be published quickly, for it is difficult to use such a vast work without the index.

A man of unassuming modesty, he found contentment in his work and in his home life. His hobbies were music and Greek literature, and he published a book on "Antike Astronomie" some years ago. Anxiety over her husband during his last illness undermined her own health and Edith Balss (née Westphal) died two days before him.

ISABELLA GORDON

NEWS and VIEWS

National Institute for Research in Nuclear Science: Rutherford High Energy Laboratory

THE new laboratory of the National Institute for Research in Nuclear Science, now being built at Harwell, is to be called the Rutherford High Energy Laboratory to commemorate the work of the late Lord Rutherford in the development of nuclear physics. It is to occupy a site adjacent to the Atomic Energy Research Establishment and will house the Institute's first large accelerator, a research machine of which the main part is a magnet-ring 120 ft. in diameter, weighing more than 6,000 tons.

Dr. T. G. Pickavance

DR. T. G. PICKAVANCE, who has been appointed first director of the High Energy Laboratory, is at present deputy head of the General Physics Division of the U.K. Atomic Energy Authority Research Establishment at Harwell. In that capacity, Dr. Pickavance, who is forty-two, is at present in charge of the group within the Atomic Energy Authority responsible for the design and supervision of the construction of the new large accelerator for the Institute and will continue to undertake this work. He has been working at Harwell since 1946 and has been deputy head of the General Physics Division since 1955. During 1939–46 Dr. Pickavance worked on nuclear problems as a part-time lecturer at the University of Liverpool and a member of the 'Tube Alloys' project. He read physics at the University of Liverpool and later did postgraduate work there under Sir James Chadwick.

Agriculture at Newcastle upon Tyne: Prof. Henry Cecil Pawson, M.B.E.

PROF. H. C. PAWSON has been elected professor emeritus of the University of Durham following his recent retirement after forty years of unstinted service in the School of Agriculture at King's College, Newcastle. This most recent honour, together with his election to a personal chair in 1948, are fitting recognition of his valuable contributions to agricultural research and education. Prof. Pawson is one of the most selfless of men, and among his students he has created a great respect and affection because of his sympathy and sincerity. He is, in fact, the ideal senior tutor, a post he held in the School of Agriculture for many years. His name will

always be associated with Cockle Park, of which he has been director and where for a number of years he was, as a young man, personal assistant to Prof. Douglas Gilchrist. At present he is engaged on a history of Cockle Park in order to place in perspective the substantial contributions of Somerville, Middleton and Gilchrist to modern agricultural thought and practice. Recently he has published a book on the life of Robert Bakewell, of Dishley, in which is given a most interesting series of letters written by Bakewell, towards the end of the eighteenth century, to George Culley, a notable Northumbrian farmer, who was largely responsible for the development of the Border Leicester breed of sheep. Prof. Pawson is also well known in the Methodist Church, and during 1951–52 was vice-president of the Methodist Conference of Great Britain.

Prof. T. W. Walker

Prof. Walker, professor of soil science at Canterbury Agricultural College, New Zealand, follows Prof. Pawson. Prof. Walker graduated with first-class honours in chemistry from the University of London in 1936. He was awarded the D.I.C. and Ph.D. for his thesis on "The Influence of Soil Type on the Growth of Plants". Afterwards, he was awarded a Salters Fellowship and spent two years at Rothamsted working on physical and chemical problems of soils. His research was interrupted by the War and he became interested in more immediate problems in connexion with the food production programme. In this he was closely associated with Dr. E. M. Crowther. In 1946, on the inception of the National Agricultural Advisory Service, he was appointed provincial advisory chemist for the West Midland Province, and he held this post until 1951, when he was appointed to the chair of soil chemistry in New Zealand. In his present post he has created an enviable reputation, not only for the quality of his research but also for the competent way he can interpret this work to farmers. His particular research interests in recent years have been concerned with the response of crops to minor elements, in particular molybdenum and sulphur. Prof. Walker will take up his duties at King's College at the beginning of the 1958–59 session. His chair is a newly established one, but in fact he replaces Prof. H. C. Pawson.

End of the Rocket of the First Artificial Earth Satellite

It is reported from Moscow that observations of the carrier rocket of the first artificial Earth satellite show that about midnight on November 30 the orbital period of the rocket began to diminish rapidly and it lost height. In the early hours of December 1, as the rocket passed over the areas of Irkutsk, the Chukotka Peninsula, Alaska and the western coast of North America, it re-entered the denser layers of the Earth's atmosphere and began to burn up. It is reported from the United States that the last instrumental observation of the carrier rocket was made about midnight on November 30 as it passed over western Pennsylvania. The life of the rocket carrier as an Earth satellite from its launching on October 4 was thus 58 days, in which time it had executed 879 revolutions of the Earth.

Rocket Testing Ranges

The Minister of Defence, Mr. Duncan Sandys, announced, in reply to a question in the House of Commons on December 4 regarding the Western Isles guided-missiles scheme, that after re-examining the scheme in the light of the changes in defence policy and as part of the campaign for economy in public expenditure, the Government had decided to provide in the Hebrides facilities for firing surface-to-surface rockets only. Accordingly, less land would be required in the Hebrides and the construction programme there would be greatly curtailed. Arrangements were being made to explain the position to the islanders. The review, while confirming the need for this range for surface-to-surface rockets, had shown that most of the necessary Service firings with air-to-air and surface-to-air missiles could be carried out at the Ministry of Supply rocket establishment at Aberporth and the remainder at the Army gunnery range at Ty Croes in Anglesey. Some additional instrumentation and other facilities would be required on these ranges, but the overall effect would be to reduce the capital cost of the whole scheme from about £20 million to about £5 million, with further substantial savings in running costs and in manpower. Of the £500,000 already spent on works, almost all would be required for the surface-to-surface rocket range.

Creep Tests on Materials for Gas-cooled Reactors

New research equipment designed to provide preliminary creep and stress-rupture data on metals and alloys in gaseous atmospheres at high temperatures and pressures has recently been installed in the materials research laboratory of the General Electric Company's Atomic Energy Division at Erith, Kent. Twelve creep-test units have already done valuable basic work in investigating the properties of magnesium alloys, widely employed for fuel-element cans, in carbon dioxide atmospheres. They can be readily converted for future work to deal with other materials in other gases. This equipment has been installed to meet the requirement for applied research facilities beyond the range of normal metallurgical laboratory equipment. This requirement arises from the urgency of the British nuclear power programme, which demands that investigations be carried out at a much greater pace than is usually imposed on metallurgical development work.

Photographic Observations at the Union Observatory, South Africa

Union Observatory Circular No. 116 (1957) contains seven papers, the first of which, "Photographic Observations of Minor Planets", by J. A. Bruwer, gives the positions of 163 minor planets (mean place 1950.0), followed by "Photographic Observation of Comets", by the same author. The latter paper gives the mean places of Comet Johnson (1949 ii) for five dates in August and September 1956, and of Comet Crommelin for November 7, 1956. W. S. Finsen's paper, "Photographic Observations of Mars", contains the results of some 54,000 experimental exposures during the favourable oppositions of Mars in 1939, 1954, and 1956. A selection of black and white enlargements of these exposures on 16-mm. colour film is reproduced in two plates, and colour enlargements—both paper prints and transparencies—have also been made. The best results were obtained with the 26½-in. telescope stopped down to 13½ in., using a Goerz telenegative lens and Kodachrome film. The camera was a Paillard 'Bolex' equipped with a beam-splitter or prismatic eyepiece for the visual monitoring

of the image. Selected frames from the best sequences were photographically superimposed by means of a special enlarger with provision for registration of successive frames. For black and white enlargements a 'Minus Blue' filter was used in conjunction with panchromatic film.

W. H. van den Bos contributes the remaining four papers, the first with the title "The Orbit of Rst 33", the second, "The Orbit of φ 47", the third, "The Orbit of β 430 = ψ Sgr.", and the last, "Micrometer Measures of Double Stars". The latter contains 385 measures of 165 pairs, all taken with the 26½-in. refractor.

Tropical Products Institute

THE first major removal from the Imperial Institute building in South Kensington, to make way for its demolition, will begin on December 9. The Colonial Products Laboratory will then be moving to new premises in Gray's Inn Road, London. The name of the organization is also being changed to the Tropical Products Institute in anticipation of its function broadening again to that of assisting and advising territories in tropical and sub-tropical regions which are not necessarily colonies. The building which will accommodate the Tropical Products Institute was erected in 1955 on a bombed site opposite Gray's Inn but was not originally intended for use as laboratories. It has, however, been adapted by the Ministry of Works to provide the Institute with 44,000 sq. ft. of good, modern accommodation. Eight self-contained laboratories will be devoted to advisory and research work on the main groups of plant and animal products of the tropics; the staff in these will be responsible for answering inquiries about the renewable resources of the tropics which are referred to the organization from sources at home and overseas. The laboratories together contain a quarter of a mile of benches, which will provide good average working space for the seventy-five laboratory workers that the Institute will have on its staff when it reaches full complement. Some bench space will be devoted to training overseas students and to other visiting workers. The Institute possesses a library of some 150,000 items, which constitutes a unique collection of information on tropical plant and animal products, and of the agriculture and production of the Commonwealth. Much general scientific, technological and trade information is also available. The total staff of the Institute will eventually be about 150.

Scientific Research in Schools

A JOINT Committee of the Royal Society and the Science Masters' Association has been formed to consider the problems confronting science masters and mistresses who wish to pursue research and to arrange for advice for specific research projects. The Committee consists of Sir Lindor Brown, biological secretary of the Royal Society (*chairman*). Dr. F. P. Bowden, Sir Edward Salisbury and Dr. C. G. Williams (representing the Royal Society), and Mr. W. Ashhurst, Mr. R. H. Dyball and Mr. M. C. Nokes (representing the Science Masters' Association). In order to initiate action the Committee has issued a note to teachers of science in schools and has also circularized the head masters and head mistresses of a number of schools in the United Kingdom; and eleven schools had submitted details of research projects and asked advice within a very short time after announcement. The Committee hopes to be assisted in its work by Fellows of the Royal Society and others at universities who may be willing to discuss projects with those who wish to carry out research. This kind of contact between university departments which are intimately concerned with research work and school masters and mistresses who so often feel isolated from the academic world would, in the Committee's opinion, be valuable. It is appreciated that in many schools there are neither facilities, nor has the science staff the opportunity or time, for carrying out any research; but the Committee thinks that wherever possible encouragement should be given when there is a desire by a science master or mistress to do research, as it is believed that they will themselves benefit in a number of ways and, in consequence, their teaching and their pupils will be better served.

Flow Coefficients

DIMENSIONAL theory permeates the whole field of aerodynamics. It is surprising, therefore, that it has not been systematically applied to the familiar method of metering the flow through a duct by measuring the pressure difference created by a constriction. The usual method of deducing the flow rate involves the application of an artificial correction factor (the so-called discharge coefficient) to the expression derived from an inadequate theoretical model of the flow. In a recent paper in the *Journal of Electronics and Control* (3, No. 4, 409; 1957), T. H. Redding, of the British Scientific Instrument Research Association, points out that this approach is unsatisfying æsthetically and can lead to serious misconceptions regarding the true significance of such a 'correction factor'. Instead, he applies dimensional analysis, at some length, and arrives at a more soundly based non-dimensional flow coefficient which is a function of the appropriate non-dimensional parameters that characterize the system. Whether or not hydraulic engineers take Mr. Redding's remarks to heart in this particular case, his paper demonstrates the unsatisfactory nature of the 'correction coefficient' philosophy, particularly where the teaching of students is concerned, and provides a convincing instance of the great power of the methods of dimensional analysis.

The Fossil Pigs of Florisbad

A RECENT publication of the National Museum at Bloemfontein (Researches of the National Museum, Bloemfontein, 1, Pt. 10, 239; 1957) includes a paper by Mr. R. F. Ewer on the fossil suid material recovered from the Florisbad deposit. A re-assessment of the status of *Phacochoerus venteri* and of *Phacochoerus helmei* is made, and it is concluded that *P. venteri* is not a valid species but is synonymous with *P. aethiopicus*. Also, that although *P. helmei* shows some characteristics which differentiate it from the living *P. africanus*, it is to be regarded as a local subspecies of restricted range, rather than as a distinct species. It therefore becomes *Phacochoerus africanus helmei*. The fauna suggests that the Florisbad deposits are of Upper Pleistocene age.

Applied Morphogenesis

IN a study of growth and morphogenesis in Canadian forest species, G. H. Duff and N. J. Nolan have made observations on specific increments and their relation to the quantity and activity of growth in *Pinus resinosa* (*Canadian J. Bot.*, 35, 527; 1957).

Two measures are needed to describe numerically the activity of the internodal cambium in terms of annual increment. These are 'specific wood volume increment', a measure of additive growth, and 'specific increment of cambial area', a measure of multiplicative growth. The mean area of the internodal cambium is the basis of reference for both, since it is the measure of that which is active in growth. The former measure of specific growth is numerically equal to ring width, and the manner of its factorial control has already been considered. Data for the latter are new. The geometry of the apical meristem and its products is too complex for the ready computation of specific terminal growth, but it can be shown empirically that internode length is a valid measure of apical activity. Analysis of internodal wood volume growth into its three linear components leads to the conclusion that the determinants in control of wood growth act mainly through their effect upon apical activity and upon specific increment of cambial area.

Industrial High-Speed Photography

THERE have been three international congresses on high-speed photography, held respectively in Washington (1952), in Paris (1954) and in London (1956) (*Nature*, **178**, 1440; 1956). It was felt that much might be gained if the many recent developments in techniques could be made more widely known in industry, and if the problems of industry could be brought to the attention of those working in this specialized field of applied physics. As a first step, a conference was organized by the Scientific and Technical Group of the Royal Photographic Society in collaboration with the Department of Scientific and Industrial Research, and was held at the Royal College of Science and Technology, Glasgow, on June 21. It is indicative of the present wide interest in the subject that more than one hundred people attended the conference, representing many industrial firms, Government and Service departments, and universities. After the opening address by Sir David Anderson, there followed eight technical papers. The papers presented at the conference and a résumé of the discussion have recently been published (*J. Photog. Sci.*, **5**, No. 5; 1957), providing a most valuable survey of industrial applications of high-speed photography. The conference as a whole was an outstanding success, and the organizers are to be congratulated on their work. It is most encouraging that such wide interest has been shown by industries in all parts of the country in the application of new physical techniques to their problems.

Trevelyan Scholarships

AFTER consultation between a number of industrial companies and representatives of the Universities of Oxford and Cambridge and of schools, the companies concerned are to provide financial support for scholarships of a new kind to enable selected boys to attend these universities. Dr. G. M. Trevelyan has agreed that the awards should bear his name. The Trevelyan Scholarships will be open to boys of British nationality, educated at schools in the United Kingdom, who have secured admission to one of the colleges at Oxford or Cambridge. Their value will be £450 per annum for three years, extended to four years in exceptional circumstances, and will not depend on parents' income. Financial support from industrial companies is available to ensure that twelve to fourteen scholarships can be awarded annually at each university for the initial five-year period of the scheme.

The sponsors hope that these scholarships will encourage boys to pursue a broader range of studies in the sixth form without impairing their chances of going to a university through lack of financial support. The selectors will therefore look for evidence that a candidate can both profit fully from an honours course and show that he has undertaken some exacting task or project. This might be a purely intellectual inquiry or one involving personal observation and travel. A written account of this must be submitted, together with a report on the boy from his headmaster. The first selections will be made in November 1958 by a committee consisting of representatives of the Universities of Oxford and Cambridge and of industry in equal numbers under a permanent chairman. A steering committee has been established, the members of which represent industry, schools and the universities concerned. The chairman is Sir Walter Benton Jones, and Mr. R. Peddie, of 17 Westbourne Road, Sheffield 10 (to whom inquiries may be addressed), is secretary.

Field Studies Council

THE Field Studies Council has completed its arrangements for 1958. Programmes are available of the courses at each of the Field Centres: Preston Mountford, near Shrewsbury; Malham Tarn, near Settle, Yorkshire; Juniper Hall, Dorking; Flatford Mill, near Colchester; Dale Fort, Haverfordwest; and the Skokholm Bird Observatory, Haverfordwest. The Council has a small bursary fund which is available to reduce the fees charged in individual cases of merit. Additional funds are also available through the Carnegie United Kingdom Trust to assist local natural history and scientific societies. Further information can be obtained from the Publicity Secretary, Field Studies Council, Ravensmead, Keston, Kent.

Announcements

DR. K. L. SUTHERLAND, an assistant chief of the Commonwealth Scientific and Industrial Research Organization Division of Industrial Chemistry and leader of its Physical Chemistry Section, has been awarded the H. G. Smith Memorial Medal. The Medal is awarded each year by the Royal Australian Chemical Institute to the member who, in the opinion of the Council of the Institute, has contributed most to the development of some branch of chemical science.

A SERIES of natural history lectures for junior audiences will be given by members of the staff of the British Museum (Natural History) during the Christmas holidays, starting on December 27. These lectures will be illustrated by films, lantern slides, specimens, etc., and are intended to provide something of interest for boys and girls aged 10–16 years. Further information can be obtained from the Museum Guide Lecturer, British Museum (Natural History), Cromwell Road, London, S.W.7.

AN evening reception and reunion will be held at University College, London, on February 28 from 6.30 to 9 p.m. Former undergraduates or postgraduates who entered the College during the years 1934–38 are invited. Applications for tickets (which are limited and may have to be allocated by ballot) should be made to the Assistant Secretary, University College London, Gower Street, W.C.1.

COLOUR VISION

A SYMPOSIUM on the "Visual Problems of Colour" was held at the National Physical Laboratory during September 23–25.

The opening session of the Symposium was devoted to a commemoration of the pioneer American worker on vision, Selig Hecht, who died in 1947 just after the Cambridge Conference on colour vision in which he had taken a leading part. Notable advances since then in our knowledge of the visual pigments were reviewed by Prof. G. Wald (Harvard)—a former student and collaborator of Hecht's—in his "Selig Hecht Lecture" entitled "Retinal Chemistry and the Physiology of Vision". Wald's conception of the visual pigments as a class of conjugated proteins has in recent years developed in two major directions, and, thanks to the work of W. A. H. Rushton (Cambridge), a frustration which has bothered workers on human colour vision for a long time has now in great part been removed. To deal first with the latter development, it has been proved by a completely objective method—an elaboration of the method of fundus examination with an ophthalmoscope—that photosensitive and bleachable pigments are in fact present in the foveal retina of the eye of living man. In his paper Rushton described first determinations of the absorption difference spectra and the action spectra of two such pigments, and the progress made towards identifying them with the 'pigments' inferred from psychophysical studies on normal and colour-defective subjects. The spectral curves of Rushton's two pigments have maxima at about 540 and 590 mμ respectively. The still more difficult problem of finding by the direct, physical method a possible pigment with its spectral maximum in the blue—which trichromatic ideas would suggest—remains outstanding. Only the 540 pigment was observable in the foveas of colour-defectives (dichromats) of the protanopic type, and the shape of the spectral curve of this pigment agreed well with the relative luminous efficiency curve of such subjects measured by the psychophysical method. In normals and in dichromats of the deuteranopic type, the same 540 pigment is present and, in addition, the 590 pigment, but in the deuteranope as compared with the normal the proportion of 590 to 540 pigment is greater, by a factor of about 2. This is striking direct evidence in favour of Fick's hypothesis that in deuteranopes both the 'red' and 'green' fundamental 'processes' (independent spectral sensitivities) of the normal eye are present—if in different relative amounts—and that the colour defect springs from their association together or 'fusion' so that they function as a single process. On the other hand, the explanation of protanopia as the simple lack of one fundamental process is confirmed by Rushton's results. The first steps towards exploiting the method to give information on the quantities of the pigments, their photosensitivities and the kinetics of their bleaching and regeneration have already been taken, and promise much. It should be added that the work on the fovea was preceded by similar observations on the extrafoveal retina, showing the presence there of the pigment of scotopic rod vision with properties conforming closely with those already known by other methods.

The increasing number of visual pigments for which there is evidence from studies of retinal extracts or intact retinæ was emphasized by R. A. Morton and G. A. J. Pitt (Liverpool). They note that some ten pigments, all based on retinene$_1$ as the chromophone group but occurring in different animals, have wavelengths of maximal absorption, $\lambda_{max.}$, distributed over the range 478–524 mμ, and conclude that the classification of the protein constituents of the pigments, the opsins, into scotopsins and photopsins, with the members in each group having very nearly the same properties, may need revision. In his lecture Wald put the position in the following way. Of the several known stereo-isomeric forms of retinene$_1$, only one, the 11-*cis* or *neo-b* isomer, combines with the opsins to give the visual pigments actually occurring. A second isomer, the 9-*cis* or *iso-a* form, will combine with the opsins *in vitro* to give the so-called *iso*-pigments, but these appear not to be used in actual eyes. Thus it must be differences in the opsins which account for variations in the $\lambda_{max.}$ of the naturally occurring retinene$_1$ pigments. Denton and Warren's discovery that certain deep-sea fish have visual pigments with a $\lambda_{max.}$ at about 480 mμ, coupled with very recent observations on other species of fish by Wald (see *Nature*, Nov. 9, 1957, p. 969), make it appear that the properties of fish opsins, defined say by the $\lambda_{max.}$ of the corresponding pigment, show a gradation with the depth at which the fish are normally found, from $\lambda_{max.} = 500$ mμ approx. for surface fish to $\lambda_{max.} = 480$ mμ approx. for deep-sea (200 fathom) fish. The opsins here concerned are classed as scotopsins, but the photopsins may well show a similar wide spread of properties and (Morton and Pitt) this may have implications for the pigments of colour vision. In human vision, the much greater rate of dark-adaptation of the photopic compared with the scotopic mechanism is paralleled by the more rapid regeneration, after bleaching, of the cone pigments (Rushton's observations), and this difference has in turn a correspondence with the different rates of synthesis *in vitro* of the photopic and scotopic pigments of the chicken (iodopsin and rhodopsin) from retinene$_1$ and photopsin and scotopsin respectively. Wald emphasized, however, that rate of synthesis does not necessarily distinguish photopsins and scotopsins. For example, alligator and frog visual pigments are rhodopsins, both having a $\lambda_{max.}$ at nearly 500 mμ, but their synthesis-rates differ widely. For the former, synthesis occurs with the high speed expected from photopic pigments, and the dark-adaptation of the alligator, tested physiologically, is correspondingly rapid.

The second major development of Wald's conception of the visual pigment is the stereo-isomerism of the chromaphore and its implications. In her discussion of the mode of attachment of the chromaphore to the opsin, Ruth Hubbard (Harvard) took as starting point Morton and Pitt's suggestion that a specific amino group of the opsin condenses with the aldehyde group of retinene (1 or 2) to give a Schiff base, which then, by addition of a hydrogen ion, is converted to the conjugate acid. The opsin surface near the amino group is assumed to be so shaped that only the two retinene isomers—*neo-b* and *iso-a*—which in fact combine with opsin can conform geometrically to this surface and be linked with it by secondary valency bonds along the retinene

side-chain so as to stabilize the conjugate acid in a non-acid environment and prevent its ultimate hydrolysis into opsin and retinene. At the same time, the secondary bonds reduce the lowest excitation energy of the conjugate acid to a value corresponding to the observed $\lambda_{max.}$ of the pigment. Hubbard assumes that the first result of light absorption is the isomerization of the chromaphore to the all-*trans* form which no longer 'fits' the protein surface. With the rupture of the secondary bonds, stabilization is lost, hydrolysis ensues and the final result is separation of opsin and retinene. For the exceptional case of squid rhodopsin ($\lambda_{max.}$ = 493 mμ) which in neutral or slightly acid solution is not bleached by light but is changed to an allied pigment, acid metarhodopsin, with $\lambda_{max.}$ = 500 mμ, Hubbard's explanation is that light absorption results as before in isomerization of the chromaphore to the all-*trans* form, but that the surface of this particular opsin conforms sufficiently closely to the shapes of either *neo-b* or all-*trans* isomers for both to be retained in combination with the opsin. Some difficulties were raised on the assumed effect of the secondary linkages on the excitation energy, but the further working out of this theory will be of great interest. The situation of the products of bleaching of visual pigments also arose in the paper by E. J. Denton (Marine Biology Station, Plymouth), who had studied the absorption of polarized light of different wave-lengths incident along or across the end-organs of intact animal retinæ, before and after bleaching. He found, among other things, a persistent (but not unchanging) orientation of the bleached 'chromaphore' groups lasting for about one hour. In the discussion, the suggestion that this implied a continuing attachment of the bleached chromaphore group to the opsin was not supported.

The bleaching kinetics of the visual pigments of four species of fish were found by H. J. A. Dartnall (Medical Research Council) to follow a similar course to those of frog rhodopsin, and, using the absolute spectral photosensitivity curve for the latter pigment obtained by Schneider, Goodeve and Lythgoe in 1939, the corresponding curves for the four fish species were derived. One conclusion from these results was that the quantum efficiency of bleaching is independent of wave-length in the range studied (440–580 mμ), just as for frog rhodopsin.

In two review papers, G. S. Brindley (Cambridge) and K. O. Donner (Helsinki) considered the bearing on colour vision of the latest work on the electroretinogram and the spike discharges from retinal elements. New work on frog retinæ by a microelectrode method indicated that the slow (tenths of second) variations of potential difference across the retina recorded in the normal electroretinogram are generated in a single layer of the retina from "structures which penetrate the external limiting membrane, almost certainly the rods and cones". For the human electroretinogram, a distinction between slower responses attributable to the scotopic (rod) mechanism and faster ones attributable to the photopic (cone) mechanism is well established, but the efforts made to distinguish different photopic mechanisms of colour vision—mainly by studies of electroretinogram spectral sensitivity curves—have not led to unambiguous results and are not very promising. Since the electroretinogram is, on the whole, a simple summation of responses from all parts of the large retinal area illuminated, the study of colour discrimination of a small area such as the fovea, in isolation, is likely to be defeated by the smallness of the signal obtained. By contrast, the thresholds for spike discharges of individual retinal units obtained by the microelectrode method have led to Granit's familiar dominator and modulator spectral sensitivity curves, which may well contain much of the colour-vision story. Donner showed that once we leave the scotopic dominator curve which electro-physiological, photochemical and psychophysical methods all show to be a fundamental non-composite spectral sensitivity, we have to question whether any recorded curve is not a resultant of several fundamental sensitivities arising perhaps from mixtures of different visual pigments in the same end-organs or from neural elaboration of the responses from end-organs containing different pigments. For bird retinæ, distortion of the curves by oil-drop colour filters in the cones is a further complication. Various methods must be applied to analyse recorded spectral sensitivity curves, and among recent procedures Donner described the two-colour threshold technique, and the use, as an indicator property, of the different directional sensitivities of rods and cones. Donner concludes that the broad, photopic dominator curve is produced exclusively by cone end-organs, but that it is probably a composite of more than one fundamental spectral sensitivity. The narrow modulator curves he attributes essentially to the effects of neural interaction which modify the responses of receptors with broader spectral sensitivity curves, comparable with the scotopic dominator. But he also suggests that the appearance of a modulator curve in a particular spectral region probably means that there is in action a receptor with a broad sensitivity curve peaking at that place.

The psychophysical papers showed a recrudescence of interest in the laws and representative data of trichromatic colour-matching and heterochromatic brightness-matching. Extensive measurements of the colour-mixture functions for a 10° field (Stiles and Burch, National Physical Laboratory, and N. I. Speranskaya, Moscow) have provided a possible basis for a new standard colorimetric eye appropriate to large-field colour-matching, and preliminary 'field trials' of the new data were discussed by D. B. Judd (National Bureau of Standards, Washington). Some small deviations from the additivity law for complete colour-matching were observed in the basic measurements. If appreciable deviations do occur, any selected set of colour-mixture curves must be a compromise, and for practical applications this should be one that works best for commonly occurring stimuli of continuous energy distributions, rather than for the mixtures of two or three monochromatic components normally used in measuring colour-mixture functions. G. W. Wyszecki (National Research Council, Canada) described a preliminary attack on the formidable problem of a direct determination of 'best compromise' functions from colour-matches on 115 accurately specified filter colours, and the solution by an electronic computer of an elaborate set of simultaneous equations in 32 three-component unknowns. In a contribution on the breakdown of the additivity law in direct-comparison heterochromatic brightness-matching, which is quite distinct from the additivity law in complete colour-matching, S. G. Yurov (Moscow) emphasized that it is the approach to additivity rather than the defect from additivity which is difficult to explain. However, in heterochromatic brightness-matching by the flicker method, additivity is certainly nearly true for a small

matching field. H. G. Sperling (U.S. Naval Medical Research Laboratory, New London) examined the assumption of standard colour theory that the relative luminous efficiency function V_λ is a linear combination of the colour-mixture functions, measured for the same subjects. Using the flicker method for determining V_λ he found the assumption substantially true for wave-lengths greater than about 520 mμ, but below that wave-length discrepancies of the order of 15 per cent appeared.

N. T. Fedorov (Leningrad) reported rather similar discrepancies. While the practical repercussions of these blemishes on the ideal linear and additive system of colorimetry may be slight, their causes are of considerable interest in visual theory. For a large matching field, some of the observed small breakdown in additivity (high intensities) is attributable to the intrusion of rod vision. Such effects may be expected to increase if the matching field is centred not on the fovea but on an extra-foveal point. M. M. Bongard, M. S. Smirnov and L. Friedrich (Moscow), working on extra-foveal colour-matching, 10° out from the fovea, by the method of successive instead of juxtaposed presentation of stimuli, conclude that colour-vision there is essentially four-dimensional, not three-dimensional, the fourth fundamental spectral sensitivity being that of the rod mechanism. Matches made using four primaries were stable under variations of field intensity and adaptation while the approximate matches obtainable with three primaries were not.

The matching of colours produced by stimuli applied to different retinal areas, in the same or in opposite eyes, which are in different states of colour adaptation has been actively studied in recent years, the case when only foveal (rod-free) areas are used being of particular importance. New measurements by E. N. Yustova (Moscow) of the colour changes as the foveal retina adapts to the stimulus colour itself showed the very large effects produced. In an attempt to explain a large class of these phenomena, D. L. MacAdam (Eastman Kodak Research Laboratory) was led in 1955 to postulate the operation of up to six independent spectral sensitivities in foveal vision. A new analysis by R. W. G. Hunt (Kodak Research Laboratory) showed that three may still suffice if signals in the optic nerve are not linearly related to the photochemical absorptions in the end-organs and if the non-linearity depends in a suitable way on the colour-adaptation of the retinal area. In his contribution to this symposium, MacAdam adopted a point of view close to Hunt's and with the aid of some specific hypotheses, which seem to involve the transmission of the arithmetic differences of the responses (non-linear) of different receptors, he was able to explain his original results on colour-adaptation as well as some other psychophysical data.

Several contributors stressed the importance for colour perception of the time during which the retina is exposed to a particular pattern of stimulation (C. D. Farnsworth, U.S. Naval Medical Research Laboratory). The extreme situation is reached when, by suitable optical devices, the displacements of a retinal image produced by involuntary eye movements are nullified. R. W. Ditchburn (Reading), summarizing progress in this type of experiment, showed that a desaturation of hues—in some circumstances complete—may occur when stabilization of the retinal image is not sufficiently perfect to bring about complete loss of form vision.

Although only two papers dealt with questions of noise and quantum fluctuations in retinal response, the lively discussion provoked by the views and calculations of H. Barlow (Cambridge) on the intrinsic noise in cone mechanisms showed the continuing interest in this subject.

Brief commentaries on the essentials of all colour theories (Y. LeGrand, Paris) and on subjective colour measurement (W. D. Wright, Imperial College) provided a suitable introduction to the more detailed contributions reviewed above. The proceedings—papers and discussions—will be published shortly by H.M. Stationery Office.

W. S. Stiles

SAFETY IN THE CHEMICAL INDUSTRY

A SYMPOSIUM on "Safety in the Chemical Industry", arranged by the London Section of the Society of Chemical Industry, was held during October 14–15 at the Royal Institution. The chemical industry covers an enormously wide field of activity, and safety within it bears a direct relationship to manufacturing and handling, to safe transport and further handling by those who formulate and process the products of the primary producer.

In opening the symposium, Sir George Barnett, H.M. chief inspector of factories, dealt with the frequency rate of accidents in the chemical industry and mentioned that the figure for the chemical industry as a whole is 1·43 per 100,000 man-hours worked, as compared with 1·73 for the whole of industry. He also pointed out that a number of the larger chemical firms had frequency rates which were far better than the overall picture for the whole of the chemical industry.

He said that there were certain apparent dangers associated with the chemical industry, in the manufacture of poisonous substances, in the use of high-pressure vessels, in dealing with new reagents and intermediate substances and the instability of a large number of chemical substances, and in the continual exploration of the field in which new reagents and new catalysts are being used. Sir George laid particular emphasis on the importance of chemical design in relation to the health of the process worker and the maintenance worker and also stressed the point that technical knowledge and ability, foresight and imagination are necessary in planning and design. Within recent years, much chemical plant had, in his view wisely, been housed in the open air, and he pointed out the advantages of remote control in the operation of many chemical plants.

The discipline of safety in the chemical industry is perhaps at least as far developed as in any other industry in Great Britain, and this discipline is reflected in the frequency rates of accidents. Safety, *per se*, may be divorced from the actual day-to-day training of engineers, chemists and physicists within the chemical industry, but mention was made of a special course which is now being started at the Imperial College of Science, where the general principles of safety will be taught.

With the rapid expansion of the chemical industry since the War, the problems of plant design, erection and start-up have become of major importance. The significance of dealing with materials of high toxicity was stressed by Mr. K. M. Curwen in his talk on the

erection of a plant to produce new organo-phosphorus insecticides. He very properly emphasized the problems dealing with the flow sheet stage and mentioned, as did other speakers, the importance of considering flow sheets in relation to the more modern developments, and the erection of small-scale models so that all who are concerned with safety can study the processes as they concern the workers who eventually work on the plant, and the facilities which are given to them and to the maintenance staff during periods of overhaul and replacement.

Mr. T. Wardle and Mr. B. A. Weston, of the Ministry of Supply, talked of the precautions which are necessary in dealing with explosives and the significance of the Explosives Act in what might be termed 'good management'. Their paper described the effects of blast, flame, radiant heat, crater formation and the effect of flying missiles in relation to the behaviour of explosives. They mentioned the importance of design in the building and lay-out of factories in order to prevent the propagation of explosions, and stressed the importance of the plant manager or the head of the establishment in relation to safety. They pointed out that safety officers exercise a functional control in advising on necessary safety precautions.

They laid down certain definite safety principles with regard to the handling, cleanliness and care necessary with different classes of explosives—all related to the Explosives Act—and mentioned the need for the most careful investigation into the causes of accidents in the manufacture and use of explosive substances.

Safety in the use of electricity in the chemical industry was dealt with most adequately by Mr. S. J. Emerson, H.M. senior electrical inspector of factories. Mr. Emerson spoke of the statutory regulations and the dangers of electric shock, burns, fire and eye flash. He demonstrated many of the types of electrical equipment, including flame-proof equipment, and stressed the value of new plastics as insulators of electrical apparatus. He mentioned in particular the use of polyvinyl chloride and polythene as being, in the light of present knowledge, ideal insulators, even if metallic sheathing is used for cable covering.

He discussed the alternatives to flame-proof equipment and stressed the nature of intrinsically safe circuits and safe apparatus. He also dealt with the detection of static electricity, its prevention and the problems of circuit protection, and emphasized the importance of safe earthing in relation to safety in the chemical industry—particularly where explosives and solvents are manufactured or used.

The contemporary problems of the construction of chemical plant were dealt with by Mr. G. G. Lanham, who had been associated with the construction of such plant to the value of more than £45 million. It is well known that the hazards involved in construction are among the greatest in the country, and Mr. Lanham's lecture was illustrated by a series of slides showing that, in spite of the doubling of the contractors' employees, the frequency rate of accidents had been constantly reduced over a period of construction lasting 5 years.

Mr. Lanham emphasized the importance of design and of seeking the advice of all who are concerned from the design stage, including the safety officer and the construction engineer. The three main causes of accidents are falls of persons, falling objects and handling materials. Almost a third of the serious accidents which had happened in constructing plant happened in falls from heights. He illustrated the need for bigger and better cranes to erect bigger and better pieces of equipment and mentioned that on his particular site 14,000 tons of steel had been erected in 1956 with only one serious accident. He paid tribute to the Safety, Health and Welfare Regulations of 1948, which have done much to diminish the serious accidents in the erection of chemical plant.

Mr. Lanham also mentioned the use of scale-models in design and during the stages of construction, as the information which these can give is of the greatest value.

In the final analysis, safety in the chemical industry—as perhaps in every other industry—must depend on the positive and active support of top management, and this support should be reflected at all levels of supervision down to the key personnel who are responsible for plant operation. This was stressed most effectively by Mr. S. E. Chaloner, who defined the responsibility of the plant manager and the safety officer, the foreman and those responsible for dealing with the day-to-day hazards encountered in the chemical industry. He rightly emphasized the importance of entry into tanks and confined spaces, and of opening pipe lines—a hazard which is too often overlooked—and the necessity for providing adequate protective clothing for hands, faces, eyes and feet. In common with other speakers, he dealt with the problem of fire hazards and fire prevention, particularly in dealing with inflammable solvents.

The chemical industry cannot operate safely without a completely integrated team on each plant, and this was very rightly stressed by Mr. Chaloner in dealing with the question of plant operation and maintenance. He emphasized the significance of talks being given to new entrants into the chemical industry by all who are concerned with safety and mentioned the close liaison which is necessary between the production manager, the safety officer, the maintenance staff and, indeed, the universities who train graduates in science and who could do well to run even a brief course of training in the aspects of safety in relation to future careers.

During the discussion on this paper, the importance was stressed of colour coding for pipes, to ensure that everyone concerned was aware of what any pipeline was conveying.

Mr. D. A. Yonge dealt with the difficult problem of safety in plant operation and maintenance in the petroleum refining industry. He mentioned the basic factors of safe operation in design, in training and in inspection. The petroleum industry presents particular hazards both from the point of view of toxicity, and of fire risk and explosion. He emphasized the significance of taking adequate precautions in repair work, particularly when men have to enter confined spaces, and outlined the procedure for cleaning and freeing plant of gas, and bringing it into a suitable state for maintenance and repair. He outlined the 'permits to work' system, which must obviously be an important part of management in relation to work in the chemical industry. Apart from the necessity of permits to work, the problems of using flame-free tools was raised, and these are obviously of prime necessity in the petroleum industry.

Mr. A. Webster, of the Ministry of Supply, dealt with the problems of safety in the transport and storage of chemicals and mentioned the dangers which might be encountered in the handling of toxic

materials by inexperienced people. He stressed the importance of correct labelling, a matter which has received particular attention from the Association of British Chemical Manufacturers, and he brought out particularly the importance of drivers being instructed as to the method of dealing with any particular problem, when transporting materials by road.

Mr. Webster discussed the question of storage of chemicals in tanks and emphasized the need for generous tank space where possible and of having spare tanks available for the transfer of liquids. He was against the storage of liquids of a dangerous nature in overhead tanks, and felt that those who have to store dangerous materials would be well advised to discuss their problems with the local fire services, who might at any time be called in to deal with serious fire or explosion hazards.

Mr. J. Eyers gave a most illuminating history of engineering inspection since the 1850's. He mentioned the activities of various organizations covering the risks of explosion and break-down of engineering plant, together with the perils connected with transport and erection of plant and loss following break-down. Mr. Eyers illustrated this lecture with a large number of lantern slides and outlined the philosophy of engineering inspection during the last century. He pointed out the increasing use of pressure vessels designed to operate at high temperatures and mentioned the new materials which have come to play so great a part in the changing conditions of modern industry.

He devoted considerable time to the use of X-rays and gamma-rays, together with flaw detection equipment in plant examination, and analysed the problems of surveying nuclear reactor vessels.

As did other speakers, he stressed the importance of breakdowns and explosions which were due to simple faults in design and operation and pointed out that these could be avoided if more thought were given to the early stages of plant design.

Dr. A. J. Amor dealt with the medical aspects of safety in the chemical industry and the need for careful toxicological assessment of the nature of new substances to be manufactured. He emphasized that only by biological experiment could the toxicological properties of any chemical substance be determined, and that such experiments would in the main give some sound idea of the dangers which would be inherent in the manufacture so far as human beings were concerned. He stressed the significance of toxicological research, plant design and layout, education, discipline and training, and all methods of detection and analysis—particularly in view of the problems of environmental control upon which safety in the chemical industry really depended. Discipline in working in the chemical industry was very important.

He stated that, as the health of workers in the industry was of prime consideration, it was right and proper that the doctor in industry should have at his disposal all the special diagnostic facilities which enable him to maintain a constant control on the health of people engaged in the manufacturing processes. The plant manager and his staff, the safety officer and the doctor, all have their part to play in protecting the health of chemical workers.

Mr. R. J. Sherwood discussed the problem of manufacture and handling of radioactive substances and described their unique toxic properties. A comparison of the methods employed in the manufacture and use of radioactive substances could be made to the strict discipline of the operating theatre, where the nature of the biological hazards was similar to that of radiation hazards in being unseen but yet dangerous.

Mr. Sherwood mentioned the readiness with which sources from outside the body could be calculated and measured and the need for protection in terms of protective clothing, discipline in terms of laboratory and other work and the strict necessity for correct labelling and safe transport.

SCHOOL NATURAL HISTORY SOCIETIES EXHIBITION

A LARGE crowd of schoolchildren and their teachers gathered in the Lecture Hall at the British Museum (Natural History) on October 12 for the Ninth Annual Exhibition of the Association of School Natural History Societies. The main item on the programme, apart from the Exhibition itself, was a lecture on "Dinosaurs", given by Dr. W. E. Swinton. The younger members of the audience, for whom the term dinosaurs previously had little precise meaning, soon learned from the lucid explanations given by Dr. Swinton the variety of extinct reptiles of this type. His account of our present knowledge of the subject was followed by extracts from films in which, by animated models, the living appearance of the reptiles was realistically simulated. But the audience was reminded by Dr. Swinton's commentary that the scenes occasionally departed from modern ideas on the behaviour of the reptiles.

As in previous years, the Lecture Hall was well stocked with displays by member schools. There was on display a wide variety of common and not-so-common living animals and plants, locusts, liverworts, eyed lizards, lepidopteran larvæ and pupæ and pond life in profusion. There were also the careful and detailed accounts of ecological studies—a rookery survey by Bishop's Stortford College, a variety of bird records by Felsted School, an account of the distribution of *Pleurococcus* on tree-trunks by the William Grimshaw School, London, surveys of Hilbre Island (Buxton College), Alderney (Ackworth School), the Loughborough district (Limehurst Natural History Society, Garendon School) and Stoke Woods, Exeter (Hele's School, Exeter).

Foreign natural history, too, was well represented this year. The Hertfordshire and Essex High School for Girls, Bishop's Stortford, had a live praying mantis from Israel. Felsted School displayed Nigerian insects, and from Breeks Memorial School, Ootacamund, India, came an unsolved geological puzzle. In the beds of streams on the Nilgiri plateau are found pebbles of fossilized coral, yet there are no sedimentary rocks in the vicinity.

There was ample evidence of work in the laboratory as well as in the field. Lord Wandsworth College, Basingstoke, had compared wing area and body-weight of related species of flying and flightless water beetles. Bishop's Stortford College demonstrated an elegant apparatus for measuring the respiration-rate of cryptozoic fauna. Respired oxygen was replaced by electrolysis of a copper sulphate solution, the amount of oxygen absorbed by the animal being determined by daily weighings of the copper-plated cathode. Plant-breeding experiments on the inherit-

ance of flower colour in *Mirabilis jalapa* (belle-de-nuit) were illustrated by Glyn Grammar School, Cheam. Work in the kitchen was demonstrated by a keen mycophagist, who had prepared a range of dishes from locally collected specimens. No one was invited to, and no one attempted to, taste the delicacies.

As usual, there were supporting exhibits of specimens, charts, publications and photographs by guest contributors. This year the guests were the Amateur Entomologists' Association, the Botanical Society of the British Isles, the British Naturalists' Association, the Children's Centre of the British Museum (Natural History), the International Union for the Conservation of Nature, the Nature Conservancy and the Universities Federation for Animal Welfare.

O. N. Bishop

DEW

WHETHER dew rises or falls has long been disputed: observations, recently described by Dr. J. L. Monteith (*Quart. J. Roy. Meteor. Soc.*, **83**, 322; 1957 have now been made which show that it can form in either way depending, roughly, on whether the air is calm or not.

The amount of dew formed on various kinds of surface has been measured by numerous workers. The difference in Dr. Monteith's work is that he measured the evaporation from, and condensation on, a block of turf-covered soil by continuous weighing. The formation of dew on turf adjacent to the block was observed by lightly brushing it with the back of the hand, and the weight of dew, when it was sufficient for measurement, was obtained by absorbing it on filter paper and weighing immediately against dry paper.

In the day the grass remained dry and the balance showed a loss of weight owing to evaporation. If temperature fell rapidly after dark the balance showed a continuing loss of weight for about an hour, even though moisture was visibly forming on the grass. Two states were found to occur during nights in which a measurable amount of water condensed on the grass: (*a*) one in which the rate of increase of weight of the block of soil was at least an order of magnitude less than the weight of condensed water; and (*b*) one in which the increase in weight of the soil was of the same order of magnitude as the weight of condensed water on the grass.

The first state, in which the downward transfer of water vapour from the air above must have been very small and the water evaporating from the soil all condensed on the leaves, was associated with a wind of less than 0·5 m./sec. at 2 m. above the ground. The second state was associated with slightly stronger winds, the weight of condensed water reaching a maximum with a wind of 2–3 m./sec. at the 2 m. level. With stronger winds, dew formation became less because cooling of the grass was reduced by the heat transferred downwards by turbulence being more nearly equal to the rate of loss of heat by radiation. The first state is termed by Monteith 'distillation' and the second 'dewfall'. The rates of condensation varied in each type according to circumstances, but were of the same order of magnitude, ranging from 0·6 to 2·7 mgm. cm.$^{-2}$ hr.$^{-1}$. The air within the grass-cover remained unsaturated during these states, with relative humidities of the order of 91–95 per cent. The leaves were about 1° C. colder than the surrounding air. If the air in the grass-cover became saturated, fog always formed. The maximum amount of dewfall measured during a night was 12 mgm. cm.$^{-2}$, and it is estimated that there are only some twenty nights a year at any one place in Britain at which it reaches 10 mgm. cm.$^{-2}$ and that the annual amount does not exceed 1/5 in. In warmer climates dewfall can be greater.

The paper gives a quantitative study of the whole phenomenon, including the temperature, humidity, and variations in surface-heat balance. The variations in heat-balance confirm that the condensation of moisture on the grass on very calm nights represents a transfer of latent heat from soil to grass and not from the air to the grass.

LONG ASHTON RESEARCH STATION

REPORT FOR 1956

THE annual report of the Agricultural and Horticultural Research Station for 1956 (pp. 180+11 plates. University of Bristol, 1957) summarizes another year of steady progress in research. The Pomology and Plant Breeding Section records that three families of blackcurrant seedlings raised in 1947, with the object of producing late-maturing varieties with high ascorbic acid content, fruited for the first time in 1956. Some had ascorbic acid contents of 250 mgm./100 gm. The blackcurrant breeding programme has been enriched by further additions of *Ribes* species, which now number more than one hundred. Research on the application of growth substances to fruit thinning has been continued. Striking differences in growth and leaf nutrient status of young apple trees were found in the cover-crop trial. Compared with clean cultivation, the cover-crop markedly depressed tree vigour and leaf-nitrogen status. Satisfactory seasonal control of lime-induced chlorosis of pears was obtained by sub-soil injection of 20 gm. iron per tree as iron-hydroxyethylethylenediaminetriacetic acid, or by foliar sprays of this chelate at 0·1 per cent concentration. Preliminary experiments were also made with some new iron chelates. The Entomology Section has continued investigations into the study of the fundamental effects produced by the incorporation of surface-active agents as spray supplements and the results indicate that phytotoxicity varies considerably with both the chemical structure of the wetting agent and the nature of the leaf surface. The most important factor appears to be the complex formed between the surface-active ions and the long carbon-chain alcohols present in leaf waxes. The development of spray machinery has continued with special reference to the requirements of certain tropical crops. A new list of cider apple varieties recommended for planting has been prepared jointly by the National Agricultural Advisory Service and the Station Orcharding Committee and is printed in the report. This list, which supersedes that published in 1948, is divided into varieties which are recommended and those which may be useful for special purposes. The latter group includes varieties which have some disadvantages but also some outstanding qualities. Suitable pollinators are also listed which will be of assistance in planning new orchards by modern methods.

ENHANCEMENT OF VITAMIN B_{12} ABSORPTION BY SUBSTANCES OTHER THAN INTRINSIC FACTOR

By SAMUEL M. GREENBERG, JOHN F. HERNDON, EDWARD G. RICE, EDWIN T. PARMELEE, JOHN J. GULESICH and EDWARD J. VAN LOON

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VITAMIN B_{12} absorption has been assumed to be limited by the level of intrinsic factor present in a test animal[1]; however, with massive doses, diffusion through the intestine has been observed to occur[2]. Recently, a preparation*, free of intrinsic factor, was observed to increase the absorption of vitamin B_{12} in healthy young and old humans[3]. In our laboratories a similar enhancement of vitamin B_{12} absorption was observed when this preparation was administered to either normal or B_{12}-deficient rats. A formulation (modified 'Liptril'), similar to the commercial preparation in all respects except that vitamin B_{12} was omitted, was prepared for the vitamin B_{12} absorption studies in rats. A 15 per cent alcohol–water solution served as a control. Vitamin B_{12} was added at equal levels to the two basal solutions for single daily oral intubations of the rats. The solutions were administered five times weekly for approximately two weeks to animals fed and given tap water *ad libitum* throughout the test period. Twenty-four hours after the last dose was administered, blood samples were obtained from each rat by cardiac puncture. Serum B_{12} levels, which were determined microbiologically[4], are presented in Table 1.

Table 1. SERUM B_{12} LEVELS 24 HR. AFTER THE FINAL DOSE OF MULTIPLE ORAL VITAMIN B_{12} ADMINISTRATIONS

Group No.	Vehicle*	No. of rats	B_{12} dosage μgm./day	Days administered	Serum B_{12} levels† μμgm./ml.
			Stock rats		
1	15 per cent alcohol–water	6	2·5	10	303±16
2	Modified 'Liptril'	6	2·5	10	391±17
			B_{12}-deficient rats		
3	15 per cent alcohol–water	8	1·0	9	153±14
4	Modified 'Liptril'	7	1·0	9	277±20

* Modified 'Liptril' (B_{12} omitted).

† Includes standard error of the mean; group 2 versus 1, $P < 0{\cdot}01$; group 4 versus 3, $P < 0{\cdot}001$; calculated by Student 't' test.

The first experiment indicated that rats could be used as test animals for the identification of the active ingredient in the preparation under study. In order to simplify the study, the Schilling test for measuring vitamin B_{12} absorption in humans[5] was adapted to the rat. The method, as modified, consisted of administering *per os* 0·54 ml. of water containing 1·36 μgm. (0·031 microcuries) radioactive cobalt-60 B_{12} combined with 2·16 ml. of test sample to fasted, intact stock rats. One hour after the oral dose of radioactive B_{12} a flushing dose of 100 μgm. 'cold' B_{12} was administered intramuscularly. Urine samples were collected over a 24-hr. period, digested with nitric acid and concentrated for measurement of radioactivity in a deep well scintillation counter. The fraction of the oral dose of cobalt-60 B_{12} found in the urine sample was considered as the percentage of B_{12} absorbed. A systematic analysis of 'Liptril' was made, using the described modified Schilling test, to determine the active component, or components, responsible for the enhancement of vitamin B_{12} absorption. D-Sorbitol was found to be the active agent.

The kidneys of rats have been observed to store a higher percentage of radioactivity after an oral dose of cobalt-60 B_{12} than does any other tissue[6]. Kidney storage-levels of cobalt-60 B_{12} were therefore used in our study as a second index of B_{12} absorption. In this experiment, intact fasted stock rats were orally administered 1·4 μgm. (0·037 microcuries) of cobalt-60 vitamin B_{12} in 0·54 ml. of water with 2·16 ml. of the test solution on two consecutive days. The kidneys from the exsanguinated rats were removed 48 hr. after the second dose of test solutions. The kidneys were solubilized and radioactivity was read in a deep well scintillation counter.

The results of both the modified Schilling test and the tissue storage level test are presented in Table 2. In both tests, the 28 per cent D-sorbitol solution caused a significant increase in vitamin B_{12} absorption in the normal, intact stock rat.

After finding that D-sorbitol would enhance vitamin B_{12} absorption, we tested a number of other carbohydrates for this property. We have found that only certain of the carbohydrates tested had the ability to enhance B_{12} absorption; namely, D-mannitol, L-sorbose and D-xylose. Carbohydrates that failed to enhance B_{12} absorption included sucrose, D-galactose, D-glucose, D-fructose and D-mannose.

Latner[7] has noted that the intrinsic factor is a mucoprotein or a mucopolypeptide containing a high percentage of such carbohydrates as hexosamine, fucose, galactose and other reducing sugars. Our findings suggest that the carbohydrate portion of the

Table 2. RADIOACTIVE VITAMIN B_{12} ABSORPTION MEASURED BY MODIFIED SCHILLING AND TISSUE LEVEL TECHNIQUES

Group No.	No. of rats	Vehicle for cobalt-60 B_{12}	Per cent oral dose of cobalt-60 B_{12}* Exp. 1 Schilling test (per cent excreted in urine)	Exp. 2 Tissue storage level (per cent stored in kidneys)
1	8	28 per cent D-sorbitol	7·0 ± 0·6	—
2	8	Water	2·2 ± 0·3	—
3	7	28 per cent D-sorbitol	—	6·3 ± 0·7
4	7	Water	—	2·2 ± 0·6

* Relative absorption values including standard error of the mean. In the Schilling test $P < 0{\cdot}001$; in the tissue-level test $P < 0{\cdot}01$.

* 'Liptril', commercial product, Smith, Kline and French Laboratories, Philadelphia 1, Pennsylvania, containing 15 per cent alcohol, 166·8 μgm. vitamin B_{12}/100 ml. and the following (gm./100 ml.): betaine, 14; choline citrate, 3; inositol, 3; riboflavin, 0·012; pyridoxine hydrochloride, 0·04; nicotinamide, 0·14; ferric pyrophosphate, 0·70; caffeine citrate, 1·296; D-sorbitol, 28; plus preservatives, colours and flavours.

intrinsic factor may play the major part in effecting B_{12} absorption. Assuming that the active carbohydrates and the intrinsic factor are activating similar absorption mechanisms in the gut, these carbohydrates should make excellent tools for investigating the B_{12} absorption mechanism.

With the facts that are now available, it is felt that at least two theories of the mechanism of action of D-sorbitol and of the other active carbohydrates in promoting vitamin B_{12} absorption are possible: (1) the formation of B_{12}-carbohydrate complex with the resulting protection of the vitamin from more rigid binding with other substances, or (2) the stimulation of an absorption mechanism in the gastrointestinal tract.

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AN EXPERIMENT ON 'TELEPATHY' USING TELEVISION

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THREE variants of perception without the aid of the known senses are commonly distinguished: 'clairvoyance' (extra-sensory perception of unwitnessed events), 'telepathy' (extra-sensory perception of events witnessed by a human agent) and 'precognition' (extra-sensory perception of future events, either in a context of clairvoyance or of telepathy). Although claims concerning these were considered by the majority of the contributors to a recent symposium[1] to deserve serious attention, they are still viewed with suspicion, the three main reasons being: (1) a phenomenon is claimed for which no one has yet suggested a convincing material basis; (2) such claims have traditionally been the preserve of superstition and crankery; (3) the phenomena elicited under experimental conditions are usually of small absolute magnitude, however long the statistical odds may be made by the sheer weight of the number of trials conducted in a given experiment; moreover, the conditions under which they can be reliably and consistently repeated have yet to be found.

In our opinion the first two reasons may be dismissed out of hand, for they could equally have been urged against many newly discovered phenomena which were later shown to be both real and important, for example, hypnosis. The third reason is a weighty and serious one. We ourselves are inclined to put it even more strongly: so long as extra-sensory perception remains a 'marginal' phenomenon it will matter little whether it is real or not. For even if it is real, experimentation along traditional lines is unlikely to lead to a causal analysis, and hence to control, of the phenomenon.

Faced with a similar impasse, investigators in other fields have found success along two main lines of attack, namely, selection of material on the basis of preliminary tests, and transformation of unselected material by special treatments. The stage hypnotist bases his success on his ability to pick from a large audience a few hyper-suggestible individuals; the psychiatrist can render almost any individual hyper-suggestible with the aid of the appropriate drugs.

The development of broadcasting, in particular of television, offers an opportunity of applying the method of selection or 'screening' on a mass scale. We have made a small-scale trial with the object of testing any generalized extra-sensory perception effect and looking for individuals with strongly manifested telepathic abilities who could then be made the subject of further experimental investigation. The results, of which a detailed account has been published elsewhere[2], are summarized below.

The 'screening' experiment was carried out on the evening of April 19, 1956, during a programme produced by Science Television, Ltd. After a brief explanatory discussion, one of us (D. J. W.) introduced to the audience the 'agent', Mr. G. W. Fisk, who was to retire from view and look at a series of 20 picture cards, keeping time with a signal given at 5-sec. intervals. The viewers were informed that the cards would be drawn at random from a pack consisting of three types, depicting a canoe, a wheelbarrow and a trumpet respectively. They were asked to record their guesses on a form printed in the *TV Times* and post it to the programme contractors.

1,367 completed records were received, transferred to punch cards and mechanically sorted. The pooled results showed no significant deviation from chance expectation. But one entry, submitted by a Mr. B. Downey, with 15 guesses correct out of 19 (the first card was a 'dummy') was considered sufficiently suggestive to justify further tests.

Apart from two runs each of 25 guesses with a 'Zener' pack, the results of which were negative, the further tests were conducted with a pack of 12 clock cards[2]. Each card showed a clock face with a single hand pointing to one of the 12 hours. The expected average divergence of guess from target is thus 3, with a minimum of zero and a maximum of 6.

These tests occupied a period of several months and comprised 239 guesses. In some tests the agent was in the same room as Mr. Downey in his home in Burton-on-Trent. In others the agent was in London and the percipient was in Burton-on-Trent. In 13 tests G. W. Fisk, and in 15 tests D. J. W., acted as agent. The identity of the agent in the 'distance tests' was always known to the percipient. The tests were eventually terminated because of the increasing apathy of Mr. Downey, who felt that no results of interest were accruing.

Analysis of the results by one of us (D. M.) showed no significant difference with either agent between

'distance' and 'same-room' tests. But there was a highly significant difference ($P < 10^{-3}$) between agents. The 132 guesses made with D. J. W. had an average divergence of 3·09 ($P > 0{\cdot}5$). But the 107 made with Fisk (who had been the agent in the original 'screening' experiment) averaged 2·21 ($P < 10^{-5}$). This rate of scoring is comparable in magnitude with the effects reported by other workers in tests with specially gifted subjects[4]. It was maintained when the distance tests were viewed in isolation, and these were sufficiently numerous to be significant in their own right at the 1 per cent probability-level. This is in agreement with earlier work, and suggests that the emission of information by the agent is not like the emission of unbeamed radio or light signals, which fall off in intensity in proportion to the square of the distance.

The effect was in part due to an increased frequency of 'direct hits' (zero divergence), and in part to 'near misses' (that is, greater frequency of small than of large divergences between target and guess). This result adds another item to the list of phenomena which telepathy apparently does not resemble: it is not like the performance of a man trying to read a series of symbols in a completely dark room intermittently illuminated by a good light, unless he deliberately adulterates his direct hits with near misses. It is more like that of a man trying to read in a half-light on the margin of visibility.

Provided that the good faith of Mr. Fisk and ourselves, all of whom at some stage had access to the records, is accepted, the results suggest that television broadcasts can be used for picking out exceptional individuals whose extra-sensory perception is sufficiently strong to make causal analysis feasible. It also seems that potential agents as well as percipients should be 'screened'.

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NOISE AND THE VISUAL THRESHOLD

THERE have been two interesting recent attempts to treat the visual threshold as a problem of discriminating a signal from a noisy background[1–4]. It is known from neurophysiological studies[5] that there is a variable resting discharge in the completely unstimulated eye. This 'retinal noise', together with any noise that may be added more centrally, forms the 'dark noise' which, on this theory, limits the sensitivity of the eye at absolute threshold. If there were no dark noise, there would be no reason why a single absorbed quantum of light should not be seen; if, however, the threshold of vision were set as low as this in the presence of dark noise, there would be a 'false-alarm rate', since the threshold criterion would be exceeded by the dark noise in the absence of external stimulation: thus the greater the variability of the resting discharge, the higher must the threshold be set to keep the false-alarm rate low. It is therefore important to know what is the average value and, more especially, the variability of the resting discharge.

The mean and variance of the resting discharge of single fibres can be obtained from direct electrophysiological studies. It would, however, be difficult to relate these figures to psychophysical thresholds and it would be useful to obtain estimates of the properties of the resting discharge from the psychophysical experiments themselves. Barlow[1,2] has tried to estimate simultaneously the variance of the resting discharge and the number of quanta necessary for vision from the shape of the frequency of seeing curve. His method is very ingenious but is also, unfortunately, rather insensitive and he was unable to estimate either of these quantities with any precision.

It is therefore very interesting that Gregory[3,4] has attempted to tackle this problem in another way. He has found that in differential threshold experiments, Weber's law:

$$\Delta I/I = C \qquad (1)$$

where C is a constant, does not hold exactly, but that when I is not too small, a much better fit is obtained by the relationship:

$$\Delta I/(I+k) = C \qquad (2)$$

where k is about 0·03 ft. lambert. In order to explain this, he supposes that r, the mean neural impulse-rate (using this term in a loose sense) corresponding to incident light of intensity I, is proportional to $\log(I+k)$. He also supposes that "the brain demands a constant fixed difference between impulse-rates arising from the comparison fields to make an intensity discrimination to a given fixed criterion". The difference between the mean neural impulse-rates is proportional to $\log(I+\Delta I+k)-\log(I+k)$, which when I is not too small is approximately $\Delta I/(I+k)$ (this can be shown by expansion in a Taylor series). Setting this equal to a constant, the observed relationship (2) is obtained.

This explanation of the empirical relationship (2) is the same as Fechner's explanation of Weber's law (1), except that r is supposed to be proportional to $\log(I+k)$ rather than $\log I$. It seems to us, however, that Gregory attaches a significance to the actual value of the constant k which it does not possess. For he says that "it is tempting to regard k as arising from the internal noise present in the system", and again that "We are tempted to regard this constant as arising from the mean internal noise in the system". The meaning of this statement is not very clear, but he seems to be arguing that, since r is proportional to $\log(I+k)$, then setting $I=0$, k is the equivalent, in light units, of the mean resting discharge. This interpretation of k is, however, incorrect, since equation (2) can be derived from any relationship of the form:

$$r = a + b\log(I+k) \qquad (3)$$

where a and b are any constants; for the constant a drops out when the difference between the two impulse-rates is taken. Gregory's interpretation of k rests on the implicit assumption that $a=0$, which there is no reason to suppose true.

A further criticism of Gregory's model is that he does not consider the variance of r. In any treatment of the threshold as a signal to noise discrimination, the variance of the response is obviously far more important than the mean. It might be possible to

interpret the slope of the regression of ΔI on I in connexion with the variance in the same way as the Weber fraction, $\Delta I/I$, can be interpreted when the line passes through the origin.

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We are inclined to agree with the model 3 proposed by Bulmer and Howarth, at least as an approximation, though we feel that to be useful it requires further interpretation. At the British Association meeting in 1956 (Section I) we put forward the following:

$$r = \eta + b \log(aI + \varepsilon)$$

$$[E(\eta) = m,\ E(\varepsilon) = k,\ \text{var}\ \eta = \tau^2,\ \text{var}\ \varepsilon = \sigma^2]$$

where r is the neural pulse-rate, I is the incident light intensity, of which a proportion, aI, is effective. It appears that nerve impulse-rate is an approximate logarithmic function of light intensity (we include the constant b since we do not know the logarithmic base). It seems to us important to distinguish between the addition of noise to the system before and after the logarithmic transform. We distinguish between 'retinal noise' (ε) which will include quantum fluctuation, and 'neural noise' (η) which will be variation in the impulse-rate due to random factors added *after* the logarithmic transform. We have introduced rather a large number of constants, some of which may not be easy to determine, because we do not want to limit our thinking to noise of retinal or 'quantal' origin. On general grounds we should expect noise throughout the nervous system, and we should like to be allowed to consider its effect. We may consider some implications of this model. The pulse-rate when I increases to $I + \Delta I$ is $r + \Delta r = \eta' + b \log(aI + a\Delta I + \varepsilon')(\eta', \varepsilon'$ from the same distribution as $\eta, \varepsilon)$ and

$$\Delta r = \eta' - \eta + b \log(aI + a\Delta I + \varepsilon') - b \log(aI + \varepsilon)$$

The distribution of Δr has a mean of approximately $b \log\{1 + (a\Delta I/aI + k)\}$, that is, $\{b\Delta I/I + (k/a)\}$, if I is not too small, and a variance V equal to

$$2\tau^2 + \frac{b^2\sigma^2}{(I + \Delta I + k/a)^2} + \frac{b^2\sigma^2}{(I + k/a)^2}$$

If we take this distribution as roughly normal, and assume that a difference is reported by the subject when $\Delta r \geqslant c$ (c being constant for a given subject in a given experiment), the value of ΔI which is recognized as different 50 per cent of the time is given by:

$$\frac{b\Delta I}{I + k/a} = c\ ;\ \text{that is,}\ \Delta I = \frac{c}{b}(I + k/a) \quad \ldots\ldots\ (A)$$

Similarly, the $2\frac{1}{2}$ and $97\frac{1}{2}$ per cent values of ΔI will be given respectively by:

$$\frac{b\Delta I}{I + k/a} + 2\sqrt{V} = C \quad \text{and} \quad \frac{b\Delta I}{I + k/a} - 2\sqrt{V} = C$$

The standard deviation of the frequency-of-seeing curve will thus be approximately:

$$\frac{1}{b}(I + k/a)\left[2\tau^2 + \frac{2\sigma^2}{(I + k/a)^2}\right]^{1/2}$$

and will increase with I.

Considering retinal noise, we assume this to be spontaneous breakdown of photochemical molecules, and the effect of the quantum fluctuation of light. At low intensities the receptors may be regarded as quantum counters, and the count as Poisson. At high intensities—and it is with these we are primarily interested—the receptors could not be expected to count individual quanta. Further, the probability of an individual receptor being stimulated is no longer small and the Poisson approximation cannot hold. The relation between σ and I could be found by considering the standard deviations of frequency-of-seeing curves obtained for differential thresholds using large I.

Equation A fits our results provided I is not too small. Not only will the approximations no longer hold for small I, but also the rod system of the retina which then becomes functional may be expected to have different constants. From such equations, retinal noise-levels may be estimated in terms of an equivalent external stimulus, k/a being given by the intercept on the I-axis.

To estimate neural noise is more difficult. An indirect method which may indicate a change in its value is the following. We take C as a fixed difference in pulse-rates, as in our previous communication, the difference being set by the number of acceptable false-positives. In the absence of an external stimulus there will be sporadic pulses, the count-rate increasing with increase in m or k. Thus the slope of ΔI against I will increase with any increase in noise. On general grounds, it seemed likely that older people might have a higher noise-level in their nervous system. We have undertaken a series of auditory and visual discrimination experiments to in-

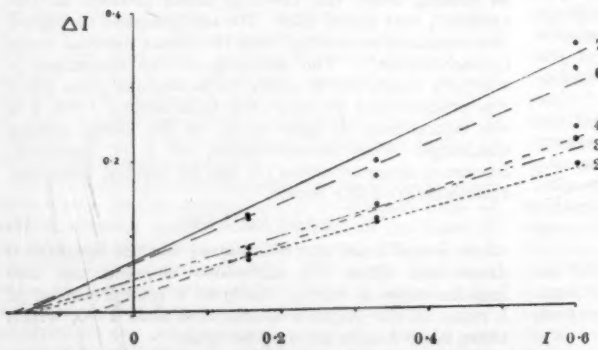

Fig. 1. Relation between ΔI and I, fitted by the method of least squares, for various age-groups. (12 subjects aged 20–30, 11 aged 30–40, 7 aged 40–50, 6 aged 70–80)
White light was used, the intensity units being foot-lamberts. The background field (I) subtended 15°, the test field ($\Delta I + I$) subtended 5°. The adjustment method of obtaining thresholds was used. Similar results have been obtained with a frequency method, employing flashes for ΔI

vestigate this possibility. We find that, for vision, slope of the line ΔI against I increases with age, whereas there is no consistent change in the intercept. Some of our results are given in Fig. 1. This suggests that neural noise (m) increases with age, whereas retinal noise (k) does not. It is interesting to consider functional losses associated with ageing as due in part to increase in neural noise. This may be supposed to affect memory storage and recall mechanisms (producing errors or delay) and also motor control, producing tremor and increase in decision or reaction time.

This at least is a crude and inadequate model; in particular, it takes no account of the level of adaptation of the eye.

We wish to acknowledge help given, at various times, by members of the Nuffield Unit for Research on Ageing, particularly Dr. J. Szafran, and also by R. T. Leslie, E. R. F. W. Crossman, A. Kendon and Miss J. Wallace, who is in receipt of a grant from the Medical Research Council, which has also made us a grant for apparatus.

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BOTH Bulmer and Howarth and Cane and Gregory accept the logarithmic relation between impulse frequency (r) and light intensity (I) expressed in the formula $r = \eta + b \log(aI + \varepsilon)$ (a, b, constants; η, ε, random variables representing neural and retinal noise), but it does not appear to be generally true in the vertebrate retina. Hartline[1] showed that it was approximately true for the compound eye of *Limulus*, and also, under more restricted conditions, in the frog[2]. These results were avidly absorbed by psychologists, because they fitted so well the logarithmic relation between sensation-level and stimulus intensity which Fechner derived by integration of the Weber law; but the maintained discharge of retinal ganglion cells in the cat does not show any such simple relation[3], and FitzHugh's results[4] suggest an almost linear relation between the number of extra impulses evoked and the quantity of light delivered in near-threshold flashes superimposed on a steady background. There may be other types of ganglion cell, not readily isolated by present techniques, which behave in a different way, but it seems rash to use the logarithmic relation in formulating a theory of visual noise.

There are two further criticisms of the formulation which Cane and Gregory now put forward. First, it fails to recognize that the variance of ε (the retinal noise which, they say, includes quantum fluctuations) must increase when I is increased. Second, so many hypothetical quantities (m, k, η, ε, c, a, b, and V) are introduced that it would be a formidable, or impossible, task to evaluate them experimentally. The complications introduced by considering a second source of noise do not seem justified until facts are found which cannot be explained by a simpler theory.

These difficulties can be avoided if one does not express noise as variance of impulse frequency. There are other possible units of measurement which can be defined as precisely, which are more easily derived from measurements of visual performance, and which may be more simply related to the cause of noise. In one of the papers[5] which Bulmer and Howarth discuss, the natural unit arising from the method is the average number (x) of random independent events (such as the spontaneous activation of a rod) which are liable to be confused with the absorption of a quantum of light: the maximum value of x was shown to be related to the number of quanta absorbed from threshold flashes and to the slope of frequency-of-seeing curves. Recently Rushton[6] estimated that 1/10 of the quanta (507 mμ) incident at the pupil are absorbed in the rods; using this figure, and previous results on absolute threshold, the method shows that x cannot exceed 10.

One might hope to compare this figure with estimates of noise obtained by different methods, and this can be done, though the comparison is not at all exact. If plausible assumptions are made[7] about the area and time within which stimulus and noise events are liable to be confused, one can calculate the intensity of a steady light which would lead to the absorption of 10 quanta, on the average, in such an area and time. This light would send about 1,000 quanta/sec. deg.^{2} into the eye, and it can be looked upon as a 'dark light' which causes noise at the absolute threshold. It should have the same value as the *Augenschwarz* of Fechner[8], the *Eigenlicht* of Helmholtz[9], and Gregory and Cane's[10] k, or k/a. It is, in fact, lower than any of them, but measurements of the difference threshold similar to those upon which the above quantities were based have been made[7,11] under conditions where rods alone are active, and these yield values for the dark light which fall in the range 200–3,000 quanta (507 mμ)/sec. deg.^{2} entering the eye. It can also be shown that the mean and the variance of frequency of the maintained discharge of ganglion cells of the cat's retina are probably compatible with such a dark light, though, as Bulmer and Howarth point out, there are difficulties in relating the two.

These three otherwise unrelated results could all be explained by a dark light of the order of magnitude of 1,000 quanta (507 mμ)/sec. deg.^{2}, and this approximate agreement provides some experimental justification for the concept of retinal noise. Furthermore, if a large part of it is caused by thermal decomposition of photosensitive pigments, one can relate the higher dark light and reduced sensitivity of cones to the shift to the red of their spectral sensitivity curves[12]. Thus the difficulties raised by Bulmer and Howarth, and the complexity which Gregory and Cane's formulation requires, are avoided if visual noise is measured as dark light, not as variance of impulse frequency. There will, however, be plenty of room for argument until the source, or sources, of visual noise are known with greater certainty.

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LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications.

Occurrence of the Meta-stable Omega Phase in Zirconium Alloys

Transformation of the retained β-phase in certain titanium alloys has been shown to involve a meta-stable phase, designated, ω. A similar mode of transformation has been reported for zirconium–niobium and zirconium–molybdenum alloys (Miodownik, A. P., and Eliasz, W., unpublished work, 1955, and ref. 2).

An extensive survey of the occurrence of the ω-phase in zirconium alloys is being carried out in these laboratories. The results to date indicate the occurrence of the ω-phase in the following alloys: zirconium–50 at. per cent titanium, zirconium–7 at. per cent vanadium, zirconium–13 at. per cent vanadium, zirconium–4·5 at. per cent chromium, and zirconium–10 at. per cent niobium. All the samples were either water- or argon-quenched from the single-phase β-region. The intensities of the X-ray diffractions have been noted to change with ageing time, indicating progressive transformation at the two ageing temperatures studied, namely, 300° C. and 400° C.

The present results are consistent with the hexagonal crystal structure of the ω precipitate first reported by Silcock *et al.*[3] for the titanium–vanadium system. However, the 'ideal' axial ratio of 0·613 has not been observed. All β quenched alloys after ageing 3–4 hr. give a value of c/a equal to $0{\cdot}622 \pm 0{\cdot}002$. It is therefore not possible to interpret the ω lattice in zirconium alloys as cubic with three times the β-lattice parameter.

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Some Properties of Chromium deposited from an Electrolyte containing Fluoride

It is well established that high-purity chromium can be produced by electrolysing an aqueous solution of chromic acid containing a small sulphate addition, and that a significant factor governing the purity of such material is the temperature of the electrolyte[1]. Oxygen and nitrogen contents of 0·02 and 0·001 weight per cent respectively or better can be attained provided the bath temperature is high, that is, in the vicinity of 80° C. Under optimum conditions the metallic impurity is extremely low.

A considerable disadvantage of this process from certain points of view is the low current efficiency (6–12 per cent) resulting from the high operating temperature. One method of overcoming this deficiency is to replace the sulphate radical in the bath by fluoride as the active anion catalyst. Thus an aqueous solution containing 300 gm./l. chromic acid (CrO_3) and 5·25 gm./l. fluoride (F), electrolysed at 100–103° C. using a current density of 800 amp./ft.^{2}, deposited chromium at a current efficiency of 40–45 per cent for 1-hr. runs in a small-scale apparatus and at 33–35 per cent in somewhat larger equipment. The reason for these greatly improved current efficiencies is not clear.

Oxygen and nitrogen contents of 'fluoride' chromium (0·02–0·05 and 0·002–0·003 weight per cent respectively) deposited under optimum conditions were not greatly different from those of 'sulphate' material. Pick-up of tin to the extent of 0·005 per cent from the 7 per cent tin–lead anode used and of silicon to the extent of 0·036 per cent by etching of the glass container by hydrofluoric acid, occurred in a 7-hr. run. The latter result emphasizes one of the difficulties inherent in the 'fluoride' process, namely, the choice of materials to contain the reactive electrolyte. For large-scale application, and to minimize pick-up of silicon, it would probably be necessary to replace glass vessels by a suitable plastic. The other major difficulty encountered was the necessity to fit the cell with reflux condensers to minimize evaporation losses from the boiling electrolyte.

It was found that 'fluoride' chromium could be arc-cast, extruded, swaged and rolled without difficulty using a similar schedule to that already reported for 'sulphate' material[2,3]. This being so, it was possible to compare the properties of wrought and of recrystallized samples of each material. Ductile/brittle transition temperatures obtained in slow, three-point bending are presented in Table 1.

Table 1. Transition Temperatures of 'Sulphate' and 'Fluoride' Chromium

Material	Composition (weight per cent)		Transition temperature (° C.)	
	Oxygen	Nitrogen	As rolled	Recrystallized
'Sulphate' chromium	—	0·002	−60	380
	0·012	0·001	—	195
'Fluoride' chromium	0·025	0·002	−87	121

Thus the transition temperature of 'fluoride' chromium is lower than that of 'sulphate' chromium in the wrought, and particularly in the recrystallized, condition. This applies even though the nitrogen content, which has been found previously to have a profound effect on transition temperature[3], is higher for the 'fluoride' chromium than for one of the 'sulphate' samples. It is possible that this improved ductility results from an action of the silicon present in modifying the detrimental nitrogen effect, which it is believed may arise either by the formation of Cottrell atmospheres around dislocations or by precipitation in dislocation lines following atmosphere formation[3]. It is to be expected that such modification by 'nitride-formers' would be more pronounced in recrystallized than in wrought material since high-temperature annealing would provide opportunity for 'nitride-formers' to develop their maximum effect. Nevertheless, even in recrystallized 'fluoride' specimens strength is dependent on temperature, and yield points were detected at temperatures where the material becomes deformed plastically.

This indicates that Cottrell locking effects had not been eliminated.

As a complementary ductility evaluation, a room-temperature tensile test was made on a specimen machined from a swaged rod of 'fluoride' chromium having a gauge diameter of 0·115 in. and a gauge length of $4\sqrt{A}$ (A = cross-sectional area). Ductility figures of 57 per cent elongation and 55 per cent reduction in area were obtained, which compare favourably with values of approximately 40 per cent elongation and 50 per cent reduction in area achieved on a specimen of similar size and condition prepared from 'sulphate' chromium.

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Corrosion as affected by a Zone of Metal emerging from the Corrosive

It is well known that 'water-line' corrosion is caused, and salt-spray corrosion is facilitated, by the easy access of oxygen to the metal through the three-phase boundary between the metal, the electrolyte and the atmosphere. The experiments described below give some insight into the mechanism of the arrival of oxygen at such menisci and its electro-dissolution.

When a metal is partly submerged in an electrolyte, which may or may not wet the metal, the surface may be regarded as consisting of four distinct zones: (A) The completely submerged area not immediately adjacent to the water line. (B) A narrow band just below the water line. Oxygen reaches this area by dissolving near the meniscus and diffusing along a short path of electrolyte, and at this position it can be cathodically reduced. (C) A band just above the water line. It is the object of this communication to show that this area can play an important part in supplying zone B with oxygen. (D) The area above C, which is of no interest, since it plays no part in the corrosion reactions.

If the metal is corrodible, A, or sometimes the uppermost part of A only[1], becomes an anode, and is attacked, while B (and obviously C and D) remain unaffected, though B and C participate in the mechanism. When the atmosphere above the electrolyte is air, zone C is narrow, and its action is not easily separable from that of B, but in an atmosphere which is more tenuous in oxygen than is air C can spread out to regions far above the meniscus.

The part played by the various zones can be simply demonstrated by coupling a strip of relatively inert metal (such as platinum, silver, nickel, stainless steel, or titanium) as cathode with a large area of a moderately base metal (such as lead, cadmium or iron) as anode in an electrolyte (potassium hydroxide, sodium chloride). The base metal must not evolve hydrogen. The anode and cathode are connected through a current-measuring system of low resistance. So long as the cathode is completely submerged in the stagnant solution (case A) the galvanic current measured, i_A, is largely controlled by the rate at which oxygen diffuses from the bulk of the solution towards the cathode. It is therefore little dependent on the nature of the cathode material. If the level of the electrolyte is now lowered until the upper edge of the cathode *almost* emerges, a zone B is created, and a rise of current, to $i_A + i_B$, is observed. If the meniscus is further lowered by 1–2 mm., so that the upper edge of the cathode begins to emerge, the current rises very steeply to $i_A + i_B + i_C$. The ratio i_C/i_A depends on the nature of the cathode material and electrolyte: it is much larger for platinum or silver than for stainless steel or titanium. Under an air atmosphere a further move downwards of the meniscus does not increase the total galvanic current; the portion i_A actually becomes smaller as the area A diminishes.

Under an atmosphere of nitrogen, but with oxygen still dissolved in the solution, $i_C = 0$, while i_A decreases linearly as the water line descends. If the electrolyte is de-aerated and the atmosphere contains only small portions of oxygen, $i_A = 0$ but i_C is relatively large, and the width of band C is found to be much wider than under air. Fig. 1 illustrates this difference: the cathode used was a sheet of bright silver bent into a cylinder 3 cm. high and 6 cm. in circumference, giving a meniscus 12 cm. long. The anode was metallic cadmium electrodeposited into porous nickel, and the electrolyte was de-aerated 5 N potassium hydroxide. The galvanic current was recorded as potential drop across a 100-ohm. load: the liquid level was lowered at the rate of 1 mm./min. In this system, if air is the atmosphere (Fig. 1*a*) zone C is 2–3 mm. wide. (The total rise of current takes place over a band 4 mm. in height, but the point at which the upper edge of the silver cylinder

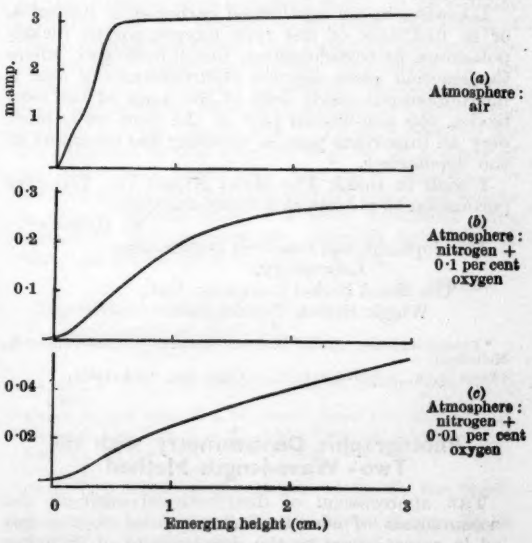

Fig. 1. Rate of corrosion as affected by the emerging part of the metal in the system: Atmosphere/silver, 12-cm. water line/5 N potassium hydroxide, de-aerated/active cadmium/100-ohm load

cuts the surface of the solution may actually lie 1–2 mm. to the right of the origin.) Under an atmosphere of nitrogen containing only 0·1 per cent oxygen (Fig. 1*b*) zone *C* spreads over about 20 mm., and at higher dilution of oxygen (Fig. 1*c*) it extends much farther.

The curves do not depend on the rate at which the meniscus is lowered, and the change may be effected in steps. A very thin film of 'Vaseline', sufficient to make the silver surface repellent to the caustic solution, does not suppress the effect of the emerging area.

Curves similar to Fig. 1 were obtained also with the system nickel/potassium hydroxide/lead. In a neutral or acid system, for example, stainless steel (18 per cent Cr, 8 per cent Ni, 1 per cent Nb)/sodium chloride/iron or alloy (40 per cent Ni, 20 per cent Cr, 3 per cent Mo, 2 per cent Cu, balance substantially Fe)/sulphuric acid/copper, the corresponding curves tend to be erratic, often with maxima and minima superimposed, and they are sensitive to point-to-point differences in the condition of the emerging surface. Also, the currents i_C are smaller and the zone *C* is rather narrower than in alkaline systems.

The mode of action of zone *C* is not clear, but it must be assumed that oxygen is adsorbed there and that in the adsorbed state it is capable of diffusing towards the water line. The thin film of water present on the 'dry' area does not appear to hinder this mechanism.

It is well known that under a droplet of spray a metal often corrodes in the centre of the droplet (*A*), rather than suffering attack at the circumference (*B*). From the above experiments it must be concluded that outside the droplet there exists a 'halo' (*C*), about 1 mm. wide, which contributes to the corrosion by acting as a catchment area for oxygen.

Similar effects must also be expected during the electro-dissolution of hydrogen at a semi-immersed platinum anode, and possibly during the corrosion of metals semi-immersed in molten electrolytes, or of steel in the nearly anaerobic atmosphere of a boiler or condenser.

Likewise, in air-depolarized carbon–zinc batteries, or in fuel cells of the type oxygen/porous nickel/potassium hydroxide/porous nickel/hydrogen, where the reacting gases dissolve electrochemically near a micro-meniscus inside each of the pores of the electrodes, the non-wetted part of the pore walls must play an important part as affecting the transport of the depolarizer.

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Photographic Densitometry with the Two - Wave-length Method

The appreciation of distributional error in the measurement of complex microscopical objects has led in recent years to the development of scanning methods of photometry and the two – wave-length method of microspectrophotometry. The two – wave-length method has been used successfully in a number of laboratories since its inception by Ornstein[1] and its elaboration by Patau[2]. It is based on an empirical correction for distributional error derived from transmission readings of the entire object taken with two wave-lengths which have been pre-determined to give true absorbances in the ratio of 1 : 2 for the chromophore being measured. The successful application of the method depends on the spectral characteristics of the chromophore, and on the presence in the object of suitable areas in which the chromophore is randomly distributed and can be measured for the selection of appropriate wave-lengths. Three types of material will not meet these requirements. They are objects without homogeneous portions, objects in which more than one independent chromophore is present, and objects in which the chromophore has too flat an absorption spectrum to supply the necessary ratio.

The photographic two – wave-length method is intended for objects falling into the above categories. The objects to be measured are photographed at a convenient magnification using monochromatic light. The resulting black and white negative is contact-printed, and the positive plate is developed with a coupling reagent. After bleaching and fixation, the positive transparency will be in one of a number of available colours and can be subjected to two – wave-length analysis. The spectral determinants are now those of the photograph, and are readily secured from a homogeneous portion of the plate. The readings may be carried out on a modified conventional spectrophotometer, or by inserting the plate into the optical train of a microspectrophotometer in the focal plane immediately below the eyepiece.

The method has been tested on photographs of stained material taken at 5893 A., or of unstained material taken at 2536 A. In the latter case, isolated rat liver nuclei have given modal distributions of total absorbance which fall in geometric progression and fit closely to the biochemical predictions of deoxyribonucleic acid content. The results with the stained material have been evaluated by measuring the same cells by the direct two – wave-length method and comparing the results with those obtained from the photographs. The two methods gave values for a population of cells which have similar variances, the same means, and a very close correlation between individuals. The photographic two – wave-length method has thus been shown to be comparable to the direct two – wave-length method.

The photographic two – wave-length method is potentially applicable to many forms of photographic densitometry, and should be of greatest value in those cases where discrete heterogeneous images are undergoing measurement.

These observations were made during the tenure of a British American Exchange Fellowship of the American Cancer Society and the British Empire Cancer Campaign, under the supervision of Prof. J. S. Mitchell.

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Intramolecular Transfer of Electronic Energy in Dihydro Diphosphopyridine Nucleotide

DIHYDRO diphosphopyridine nucleotide shows blue-white fluorescence ($\lambda_{max.}$ = 468 mμ) in water solution[1] with a quantum yield[2] of 2 per cent on excitation by mercury 366 mμ radiation. Several reduced N-alkyl nicotinamides show fluorescence almost identical in spectrum and quantum yield with that of dihydro diphosphopyridine nucleotide. The excitation spectrum of the fluorescence[3] of these reduced N-alkyl nicotinamides (Fig. 1) shows complete coincidence with the fractional absorption spectrum over the whole range of wave-lengths explored (220–410 mμ). The fluorescence-excitation spectrum of water solutions of dihydro diphosphopyridine nucleotide at *p*H 7–9 shows a further strong band with a maximum at 260 mμ, a region where 80–90 per cent of the absorption is due to the purine part of the molecule. From these observations it appears that 30 per cent of the photons absorbed by the adenine appear as nicotinamide fluorescence. The integrity of the molecule is required for this energy transfer to show itself: after a solution of dihydro diphosphopyridine nucleotide at *p*H 8·3 has been acted upon by nucleotide pyrophosphatase[4] the 260 mμ band of the fluorescence-excitation spectrum disappears, the resulting spectrum becoming similar to that of the reduced N-alkyl nicotinamides. The enzyme hydrolyses the P—O—P linkage and causes the purine and nicotinamide nucleotides to become independent molecules, which in a 9×10^{-6} *M* solution, the concentration of the experiments, are at an average distance of 300 A. of each other. Solutions of dihydro diphosphopyridine nucleotide in propylene glycol show no detectable 260 mμ band in the fluorescence-excitation spectrum, while solutions in 60 per cent sucrose in water show a 260 mμ band the intensity of which is four-fifths of that in pure water.

Observations of the polarization of the fluorescence of sucrose solutions (Table 1) show that in dihydro diphosphopyridine nucleotide, excitation with either mercury 366 or mercury 254 results in fluorescence with positive polarization which increases rapidly with the viscosity of the solvent. From the rate of change of polarization with viscosity, and using a value of 900 cm.³ for the molar volume of dihydro diphosphopyridine nucleotide in solution, a lifetime of the excited state of $0{\cdot}5 \times 10^{-9}$ sec. can be calculated[5], consistent with the low quantum yield. The values of the polarization for excitation by mercury λ 254 agree with the lifetime calculated for excitation with mercury λ 366. Moreover, they are conspicuously higher than the values obtained on excitation by mercury λ 254 of N-methyl nicotinamide in 60 per cent sucrose, or dihydro diphosphopyridine nucleotide in propylene glycol, thus showing that the transfer of the excitation energy absorbed at 254 mμ in aqueous dihydro diphosphopyridine nucleotide results in the emission of polarized fluorescence and does not lengthen appreciably the lifetime of the excited state of the nicotinamide nucleus. This excludes a metastable state of the adenine as a source of the transfer and indicates a coupled oscillator mechanism[6] as the likely one. In agreement with other authors[7] no fluorescence was observed in solutions of adenine or adenylic acid although a quantum yield of 0·1 per cent would have been detected by the method used. Thus the transfer has to compete with a radiationless transition with a probability of 10^{11} or higher (reciprocal of natural lifetime times quantum yield). A probability of transfer of 10^{11} requires short-range interaction of the molecules concerned[8] and points to the existence in dihydro diphosphopyridine nucleotide of an intramolecular complex similar to the one already described in flavin adenine dinucleotide[9] between the adenine and the *iso*alloxazine. Further evidence for the existence of this complex is given by a study of the absorption spectrum: the ratio E_{260}/E_{340} is 2·85 for intact dihydro diphosphopyridine nucleotide in water, increasing to 3·3 after treatment with nucleotide pyrophosphatase, whereas solutions in propylene glycol show $E_{260}/E_{340} = 3{\cdot}4$.

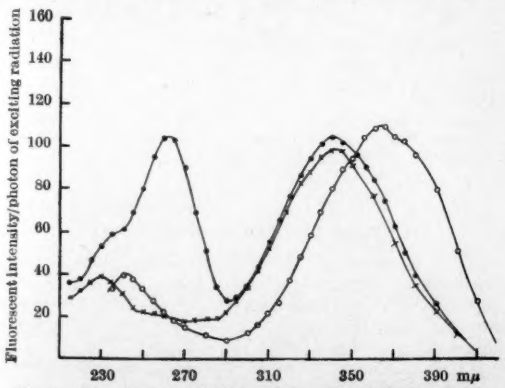

Fig. 1. Fluorescence-excitation spectra. Band-width, 1·5 mμ. Open circles, 4 hydro N-methyl nicotinamide in 0·1 *M* sodium carbonate; dark circles, dihydro diphosphopyridine nucleotide in 0·1 *M tris* buffer *p*H 8·3; crosses, dihydro diphosphopyridine nucleotide in 0·1 *M tris* buffer *p*H 8·3 after incubation for half an hour at 38° with nucleotide pyrophosphatase. The light absorption by the enzyme is negligible throughout

Table 1. FLUORESCENCE POLARIZATIONS *P* FOR EXCITATION WITH NATURAL LIGHT. OBSERVATION AT 90° TO THE DIRECTION OF EXCITATION

Substance	Solvent viscosity (centipoises)	*P* Mercury-366	*P* Mercury-254
Dihydro diphosphopyridine nucleotide in 60 per cent sucrose	55	0·192	0·055
Dihydro diphosphopyridine nucleotide in 40 per cent sucrose	6	0·158	0·04
Dihydro diphosphopyridine nucleotide in 20 per cent sucrose	2	0·091	0·025
Dihydro diphosphopyridine nucleotide in propylene glycol	56	0·159	<0·02
4 Hydro N-methyl nitocinamide in 60 per cent sucrose	55	0·105	<0·02

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Polarization of Comet Arend–Roland

When, last May, Comet Arend–Roland became a bright naked-eye object in the northern hemisphere, we carried out a series of photoelectric measures of the polarization of its coma at different phase angles. The technique employed utilized a piece of 'Polaroid' attached to a rotatable six-position disk contained in the photometer. This enables measurements of intensity to be made as the 'Polaroid' is turned through 60 deg. for each position of the disk. Standard *B* and *V* filters employed in the *UBV* system, together with interference filters having peak transmissions centred on 5890 A., 5000 A., 4700 A. and 4300 A. and half-widths of 80 A. were used for isolating the different wave-lengths. Each of the three circular apertures behind the 'Polaroid' transmitted 3·7 square minutes of arc of the sky.

We have calculated the amount of polarization and plane of polarization, from at least six sets of measures, each day, for radiation transmitted by each filter, a set of deflexions being considered as those obtained through three successive positions of the 'Polaroid'. Since, in each position of the 'Polaroid', the light reaches the photomultiplier through a diaphragm and area of the 'Polaroid' different from that of the previous position, we determined correction factors by measures of bright nearby stars, and applied these to the cometary measures. The orientation of the 'Polaroid' was determined by a laboratory arrangement, and we believe that the error in transferring this plane of reference to the telescope does not exceed 1 deg. The probable error of the value of percentage polarization is estimated to be less than ± 1 per cent and that of a value of the plane of polarization to be ± 5 deg. The values derived for 5890 A., 5000 A., and 4700 A. are given in Table 1. These values cover a limited range of phase angle because the comet, after May 8, was beyond the range of accurate measurement with our interference filter – 'Polaroid' combination.

Table 1

Date May 1957	Percentage polarization and position angle of plane of polarization		
	5890 A.	5000 A.	4700 A.
4·658	17·5 103°	—	17·9 107°
5·641	17·4 116°	18·0 112°	20·4 114°
6·648	19·7 119°	15·0 117°	17·3 119°
7·655	12·9 121°	14·1 124°	16·8 122°
8·660	20·5 123°	20·0 123°	14·5 —

The measures of polarization through the *B* and *V* filters cover a larger phase angle than with the interference filters. Table 2 contains values of the amount of polarization and the plane of polarization for each day obtained through the *V*-filter, along with those of phase angle and position angle of the intensity equator that were calculated from the emphemeris of Candy[1]. A general decrease in amount of polarization with phase angle, along with superimposed erratic fluctuations from day to day of the order of 2–3 per cent, is seen. Assuming that the relation between amount of polarization and phase angle is given by

$$P_\theta = \frac{P_{90} \sin^2\theta}{1 + P_{90} \cos^2\theta}$$

Table 2

Date May 1957	Percentage polarization	Position angle of plane of polarization	Phase angle	Position angle of intensity-equator
4·658	18·9	104°	76° 24′	37° 48′
5·641	18·3	111°	73° 47′	40° 01′
6·648	19·9	116°	71° 12′	42° 12′
7·655	17·0	119°	68° 48′	44° 16′
8·660	14·5	120°	66° 36′	46° 13′
11·656	12·8	129°	60° 41′	51° 21′
14·662	14·0	148°	55° 45′	55° 25′
15·662	15·3	135°	54° 16′	56° 32′
22·647	9·6	147°	45° 44′	62° 00′
26·650	6·2	148°	41° 54′	63° 37′

where P_θ and P_{90} are the values at phase angles θ and 90° respectively, we have calculated the values of P_{90} for the comet through the different filters. These are seen to be consistent among themselves.

The 5890-A., 5000-A., 4700-A. interference filters were chosen to isolate the Swan bands present in the spectrum of the Comet. A check on the continuum was maintained with the aid of the 4300-A. filter. The *V*-filter transmits, in the yellow and green regions, the C_2 radiations and possible sodium *D*-line emission together with the continuum of reflected sunlight. Hence, a value of the polarization of the coma determined through the *V*-filter represents a weighted mean of the percentage of polarization of the emission bands as well as of the continuum. The equality in the values of P_{90} derived through the different filters used, indicates the dominant part played by the continuum. We have had no access to spectra of the Comet taken on these days, but judging from Wellman's[2] description of the spectrum as it appeared on April 23, the emission may have been very weak during the period we observed. The polarization of Comet Arend–Roland is thus similar to that of Comet Paraskevopoulos (1941*c*) studied by Ohman[3].

Within the errors of measurement, the planes of polarization at any one time of observation obtained through the different filters are all identical. Table 2 shows that the change in plane of polarization with time is linear, though it is more rapid than the change in position angle of the intensity-equator during the same time interval.

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Aug. 6.

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Crystal Structure of Oximes

The crystal structure of *syn-p*-chlorobenzaldoxime has been determined in more detail than previously reported[1] by a three-dimensional Fourier-synthesis and two-dimensional $F_o - F_c$-syntheses. The main features of the structure are shown in Fig. 1. The hydrogen atoms connected to the carbon atoms were found in the expected positions, although their parameters could not be determined accurately. There was fairly conclusive evidence from the electron-density maps that the hydrogen atom of the oxime group is covalently bound to oxygen; the

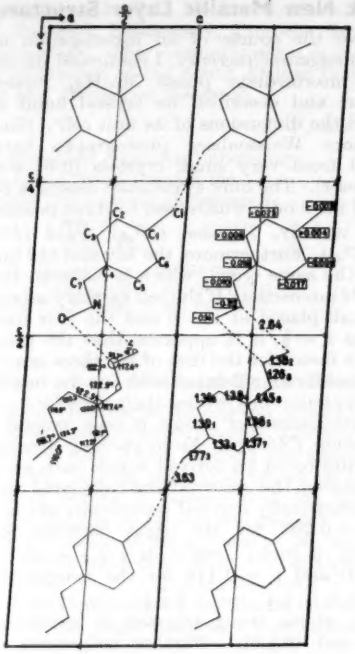

Fig. 1. *Syn-p*-chlorobenzaldoxime. The structure viewed along the *b*-axis. The interatomic distances are in angstrom units; their maximal error is estimated to be 0·04 A.

(The figures in rectangular frames indicate the distances in A. from an approximating plane through the benzene ring)

pairs of hydrogen bonds linking the molecules in dimers are thus of the type O—H . . . N.

It seems clear that in these dimers the hydrogen bonds are non-linear; indeed, two centrosymmetrically related hydrogen atoms on the straight line O . . . N at a distance 1 A. from the oxygen atoms would be only 1·7 A. apart, which is a much shorter distance than twice the van der Waals radius of hydrogen. The present observations agree with a deviation of the OH bond of about 20° from the line O . . . N. This gives a reasonable angle N—O—H of about 105°, an angle O—N . . . H′ of about 106° and a distance H—H′ of about 2·4 A.

In the crystal structure of dimethylglyoxime[2], dimerization of oxime groups in neighbouring molecules is effected by pairs of hydrogen bonds; since dimethylglyoxime is a dioxime, infinite chains are thus formed. The geometry of the oxime groups in the associated molecules is exactly similar to that of *syn-p*-chlorobenzaldoxime, thus indicating that the hydrogen bonding in the two structures is of the same type.

The crystal structure of *anti-p*-chlorobenzaldoxime has been determined from two well-resolved Fourier projections (Fig. 2), though not in so much detail as that of the *syn*-form. The *anti*-configuration of the molecule is confirmed. The oxime group is turned about 19° out of the plane of the benzene ring, presumably to avoid too close contact with C_5; resonance between the oxime group and the benzene ring is thus sterically hindered, and the C_4–C_7 bond is found, in accordance with this, to have the length of a normal single bond, whereas the equivalent bond in the nearly planar *syn* molecule is significantly shorter. Apart from this, the two stereo-isomers are identical within the experimental accuracy. The molecules of the *anti* form are linked in infinite chains by hydrogen bonds between nitrogen and oxygen in neighbouring molecules; the hydrogen atoms could not be placed at the present stage of the structure determination, and according to geometrical considerations the hydrogen atom of the oxime group could be covalently bound to either oxygen or nitrogen. However, the geometry of the chains is rather like that found in the crystal structure of formamidoxime[3], where the molecules form a three-dimensional network by hydrogen bonds in which chains formed by hydrogen bonds connecting nitrogen and oxygen in neighbouring oxime groups take part. From geometrical considerations of the hydrogen bonding in the formamidoxime structure, Donohue[4] has concluded that the oxime hydrogen is covalently bound to oxygen; by analogy with this, one may infer that in *anti-p*-chlorobenzaldoxime the hydrogen bonds are also of the type O—H . . . N.

So far, only one other oxime crystal structure has been determined, that of acetoxime[5]; again the hydrogen atoms have not yet been found in the electron density calculations, and from geometrical considerations one cannot decide whether the hydrogen bonds O . . . N, which in this case link the molecules to trimers, are of the type O—H . . . N or N—H . . . O; but the former possibility would seem more likely, since there is no characteristic difference in behaviour of this oxime suggesting a structure differing from the above.

The bond-lengths in the oxime groups in the five structures are very uniform and indicate a structure predominantly =C=N—O— with a small contribution from =C—N=O.

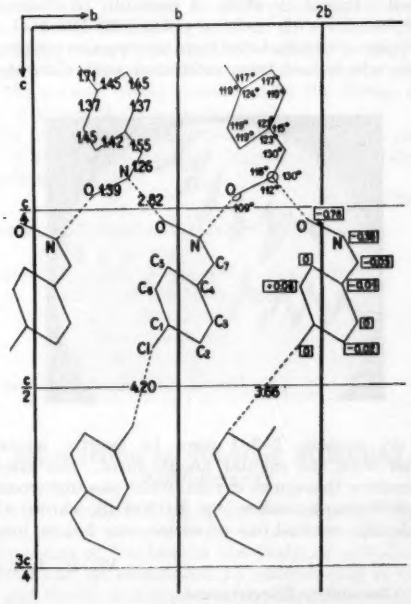

Fig. 2. *Anti-p*-chlorobenzaldoxime. The structure viewed along the *a*-axis. The interatomic distances are in angstrom units; their maximal error is estimated to be 0·1 A.

(The figures in rectangular frames indicate the distances in A. from an approximating plane through the benzene ring)

From the above results it is concluded that oximes in the crystalline state correspond closely with the classical oxime formula =C=N—OH.

It may be a general phenomenon with the aromatic aldoximes that the *syn* forms are associated in dimers and the *anti* forms in chains, as was found for the *p*-chlorobenzaldoximes. This concept is supported by evidence from infra-red absorption spectra of *syn* and *anti* forms of some aromatic aldoximes[6], and offers an explanation of the curious fact that for these oximes the *trans* forms (*syn*) generally have lower melting points than the *cis* forms (*anti*).

Two of the types of molecular association found in oximes are paralleled by the dimers and chains found in the crystal structures of carboxylic acids; the intermediate form, that is, the trimers in the crystals of the symmetrical oximes acetoxime and *cyclo*hexanone oxime[7], has no counterpart in the known structures of carboxylic acids.

A detailed account of this work will be published elsewhere[8].

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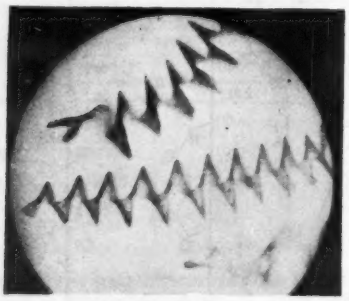
Spiral Crystals of Meconin

The growth of zinc sulphide[1] and magnesium sulphate[2] crystals in spiral form has recently been reported. Spiral crystals of meconin (6 : 7-dimethoxy-phthalide) with melting point 101–101·5° C. (lit. 102·5°)) have been isolated from an aqueous propanolic solution which had been saturated with chloroform.



Only six spirals, 2–3·3 mm. in length, appeared together with the regular needle form. An attempt to reproduce this spiral crystal form was unsuccessful. The photograph, taken by I. McGill, shows three crystals, the central one of which was 2 mm. long.

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A New Metallic Layer Structure

During the course of an investigation into the system manganese/mercury, I confirmed the existence of the intermediate phase Mn_2Hg_5 reported by Prelinger[1] and described its crystal habit and determined the dimensions of its unit cell[2]. Since then, satisfactory Weissenberg photographs have been obtained from very small crystals (0·01–0·02 mm. in diameter). The only systematic absences observed were $0kl$ for k odd, which lead to three possible space groups, namely, $P4/mbm$ (D^5_{4h}), $P\bar{4}b2$ (D^3_{2d}) and $P4bm$ (C^2_{4v}). Furthermore, the $hk0$ and $hk2$ intensities display the same trend, which is different from that of the hkl intensities. If the ten mercury atoms in the cell are all placed at $z = 0$ and the four manganese atoms at $z = \frac{1}{2}$, it is apparent that the geometrical structure factor for the first of the three space groups is identical for all reflexions with $l = 2n$, but the manganese contributions reverse their signs for $l = 2n + 1$. This arrangement of atoms is only possible in the space group $P4/mbm$. From packing considerations a structure could be derived which gave good agreement between the observed and calculated intensities. The geometrically derived parameters are $u = 0{\cdot}075$ and $v = 0{\cdot}206$ for the eight mercury atoms at positions $\pm(uv0$; $vu0$; $u + \frac{1}{2},\frac{1}{2} - v,0$; $v + \frac{1}{2}, n + \frac{1}{2},0)$ and $u = 0{\cdot}178$ for the manganese atoms at $\pm(u,u + \frac{1}{2},\frac{1}{2}$; $u + \frac{1}{2},\overline{u},\frac{1}{2})$, the two remaining mercury atoms being situated at special positions $(\frac{1}{2},0,0)$ and $(0,\frac{1}{2},0)$. Further refinement of these parameters by Fourier methods is under way; the results will be published more fully elsewhere.

The above structure leads to a closely packed arrangement in which each mercury in the (001) planes is in direct contact with its four nearest mercury neighbours in the same plane, and with one mercury atom above and below it. Each manganese atom is also in direct contact with six mercury atoms—for example, *A*, *B* and *C* in Fig. 1 and the atoms directly above them—and fits exactly into the vacant site between them.

The new metallic layer structure displays a remarkable similarity to that of tetramminopalladous chloride monohydrate, $Pd(NH_3)_4Cl_2.H_2O$ and its platinum isomorph[3]. The two extra (heavy metal) atoms per unit cell of the complex occupy the special positions (0,0,0) and $(\frac{1}{2},\frac{1}{2},0)$, which are unoccupied in Mn_2Hg_5. Although it would seem rather surprising that an alloy crystallizes with basically the same atomic arrangement as a co-ordination complex, the close packing in the structure of Mn_2Hg_5 emphasizes its typically metallic character.

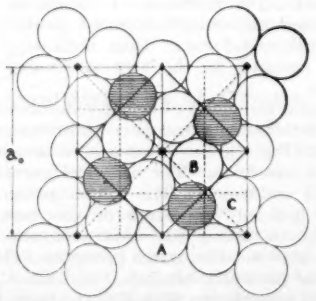

Fig. 1. Projection on (001) of the structure of Mn_2Hg_5 with two formula units per unit cell. The atomic radii taken are r_{Hg} = 1·50 A. and r_{Mn} = 1·35 A.

I am grateful to Dr. F. H. Herbstein, of the National Physical Research Laboratory, Pretoria, for stimulating discussions. This communication is published with the permission of the South African Council for Scientific and Industrial Research.

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South African Council for
Scientific and Industrial Research,
Pretoria.
July 12.

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Life-time of an Artificial Earth Satellite

IN view of the recent widespread interest in the life-time of an artificial Earth satellite, a simple expression is derived here which predicts the approximate life-time from initially measured values of the rate of change of height at apogee and the difference between the heights at apogee and perigee.

Let h be the height at perigee and $h+2h_1$ the height at apogee, both measured from the centre of the Earth. Using polar co-ordinates with r as the distance from the centre of the Earth (the assumed origin) and θ the angle measured from perigee:

$$r \sim h + h_1(1-\cos\theta)$$

and near perigee, where air resistance is much higher than elsewhere in all but the latest stage of the life of a satellite:

$$r \sim h + \tfrac{1}{2}\theta^2 h_1$$

The impact of the air molecules at any point r, θ will cause no drop in height at that point but a maximum drop in height at the diametrically opposite point, so that the ratio of the height drop near perigee to that at apogee is:

$$(1-\cos\theta)/2 \sim \theta^2/4$$

Assuming that the air resistance causes a maximum height drop proportional to $\exp(-r/H)\mathrm{d}\theta$ over the angle $\mathrm{d}\theta$, where H, the atmospheric scale-height, is assumed much smaller than h_1, the total drop at perigee during one cycle is proportional to:

$$\int_{-\pi}^{\pi} \tfrac{1}{4}\theta^2 \exp[(-h-\tfrac{1}{2}\theta^2 h_1)/H]\mathrm{d}\theta \sim \tfrac{1}{8}\pi^{1/2}(h_1/2H)^{-3/2}\exp(-h/H) \quad (1)$$

while similarly the drop at apogee is proportional to:

$$\pi^{1/2}(h_1/2H)^{-1/2}\exp(-h/H) \quad (2)$$

In view of the large decrease in the exponent of the exponential with increasing θ, there will be little contribution to the integral over large values of θ, and for simplicity the integrations were carried out from $\theta = -\infty$ to $\theta = +\infty$.

The ratio of the rate of decrease in height at perigee to that at apogee is then:

$$\mathrm{d}h/\mathrm{d}(h+2h_1) \sim \tfrac{1}{2}\mathrm{d}h/\mathrm{d}h_1 = \tfrac{1}{4}H/h_1 \quad (3)$$

Solving this differential equation:

$$h_1 = h_{10}\exp[-2(h_0-h)/H] \quad (4)$$

where h_{10} and h_0 are the initial values of h_1 and h.

The rate of decrease in height at perigee is proportional to expression (1). Substituting h_1 from (4) one obtains:

$$\mathrm{d}h/\mathrm{d}t \propto \exp[-4h/H] \quad (5)$$

the solution of which is

$$t = t_\lambda\{1-\exp[-4(h_0-h)/H]\} \quad (6)$$

The integration constant t_λ, which clearly is an approximation to the life-time of an Earth satellite, may be determined if the initial rate h'_a of losing height at apogee is known. Then the rate of loss of height at perigee is, from (3), given by $\frac{1}{4}h'_aH/h_1$, which equals, from equation (6), for very small t:

$$(h_0-h)/t \sim H/(4t_\lambda)$$

and therefore

$$t_\lambda = h_1/h'_a \quad (7)$$

This simple expression means that the life-time of a satellite is approximately equal to the time in which the distance at apogee from the centre of the Earth, decreasing at its initial rate, would reach a value equal to the initial value of the semi-major axis of the orbit. The assumption $H \ll h_1$ is of course not valid in the last stages of a satellite's life. Expression (7) is therefore an under-estimate, but if $H < 40$ km. the error is estimated to be less than 20 per cent.

From observations of the Doppler effect on the signals received from the 40·002 Mc./s. transmitter of the first Russian Earth satellite by the National Telecommunications Research Laboratory of the South African Council for Scientific and Industrial Research, the values $h_1 = 210$ statute miles and $h'_a = 2{\cdot}4$ miles/day (the latter derived from the measured rate of change of orbital period) have been obtained. From these a life-time t_λ of 87 days is obtained as from October 20, 1957.

No radio measurements are available on the rocket casing, but from time differences between the satellite and the rocket casing published in the Press, a life-time of about 56 days is obtained.

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[See page 1392 of this issue of *Nature*.]

Suppression of Bubbling in Boiling Refrigerants

DURING recent studies of the properties of radicals trapped at low temperatures it has been found that the presence of bubbles in the body of a boiling refrigerant can be eliminated by introducing a stream of a gas which is comparatively insoluble in the refrigerant. In a typical experiment a small, unsilvered Dewar flask was half-filled with liquid nitrogen at atmospheric pressure, vigorous bubbling of the liquid being observed. When a jet of helium, hydrogen, or neon gas was blown over the liquid nitrogen at a

rate sufficient to break up the surface, the bubbles at first became smaller and then were no longer visible. The liquid was now completely clear and still, and its temperature had fallen by several degrees. If the gas flow was interrupted, the bubbling eventually resumed its original intensity. When the gas was introduced 10 cm. below the surface of the liquid nitrogen instead of being blown across the surface it was found that the rate of gas flow needed to suppress bubbling was reduced considerably. In the case of helium gas, the flow could be reduced to a value of 1/6 to 1/8 of that required when blown across the surface. The introduction below the surface of nitrogen, air or argon gases, instead of helium, had little or no effect on the bubbling, so that the suppression was not caused merely by a local increase in total pressure above the surface of the liquid nitrogen.

A more detailed investigation showed that the magnitude of the drop in temperature depended only on the proportion of added gas to vaporized refrigerant, above the liquid, but not on whether the gas was helium, hydrogen or neon. Furthermore, the temperature reached by the liquid nitrogen was found to be that at which the saturated vapour pressure of nitrogen equalled the partial pressure of the nitrogen in the gases above the liquid. For example, when helium gas reduced the partial pressure of nitrogen to 47 cm. the decrease in temperature was 3·4° C., the predicted value being 3·9°. These observations are in agreement with the suggestion (Haselden, G. G., private communication) that added gases cool the liquid by reducing the partial pressure of the nitrogen.

At the lower temperature, it has been pointed out (Grassmann, P., private communication) that evaporation of the nitrogen will occur more readily into a bubble of helium than into a bubble of the liquid itself, since the partial pressure of nitrogen is initially much smaller in the helium bubble. Helium bubbles thus remove the greater part of the nitrogen evaporated, and the number of nitrogen bubbles in the remainder of the liquid is diminished.

Qualitatively similar effects were found when helium was passed into liquid air, liquid argon and liquid oxygen. Bubbling in liquid oxygen was reduced to some extent by nitrogen gas or argon gas, presumably because the gases dissolved and slightly changed the boiling point of the liquid. Oxygen gas, however, also decreased the bubbling of liquid oxygen, and the reason for this is not obvious.

The results reported here indicate that efficient suppression is obtained by using a gas with a boiling point much lower than that of the refrigerant. This method has been used in these laboratories for facilitating visual, photographic and spectroscopic observations of the condensation of free radicals and of associated processes, and other applications can be envisaged.

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Differential Thermal Characteristics of Peat

The recent extensive development of controlled-atmosphere differential thermal analysis has enabled systematic investigation of many organic materials to be carried out[1]. The data for a curve obtained from peat have indeed been quoted by Grimshaw and Roberts[1], and Kanavets, Klimov and Chibisova[2] have published two curves, one for an 'upper' (presumably a zonal or hill) peat and the other for a 'lowland' (presumably an intrazonal or basin) peat. These, however, are the only published curves we have been able to trace, and no studies appear to have been made regarding the variation in the complete-combustion differential thermal curve with respect to either botanical composition or degree of humification. From results recently obtained here it appears that the curve may be affected by both these factors.

The apparatus used was somewhat similar to that described by Grimshaw and Roberts[1], in that oxygen was passed over the sample in a porous, ceramic holder block at a rate of 200 ml./min. Samples consisted of 10 mgm. oven-dried peat diluted with 190 mgm. calcined kaolinite, the inert material being calcined kaolinite. The heating rate was maintained at 10° C./min., and photographic recording of the $\Delta T/t$ curve was employed.

Representative curves for peats of different botanical composition are shown in Fig. 1. All those examined gave rise to marked exothermic effects in the 200–400° C. region, a two-peak system usually being developed. That this is not due to incomplete combustion with successive 'bursts' of oxidation (as for pyrite in air[3]) was demonstrated by using samples of varying dilution; the peak system was found to be independent of dilution. We thus have to deal with two successive oxidations. In any event it is quite evident that the type of curve obtained is dependent upon the botanical character of the peat, and additional results have also suggested that it may be dependent upon the degree of humification.

That different fractions separated from peats also give quite distinctive curves is clear from Fig. 2. Thus the 'humic acid' fraction always gives a two-peak system with the second peak larger than the first, while the holocellulose fraction exhibits a large exothermic peak followed by two distinct groups of considerably smaller exothermic peaks. In addition

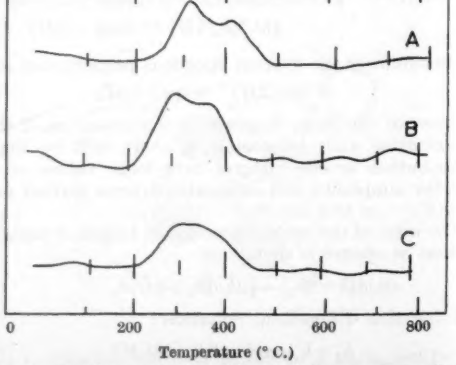

Fig. 1. Complete-combustion differential thermal curves for: *A*, *Eriophorum* peat; *B*, *Calluna* peat; *C*, sedge-grass peat

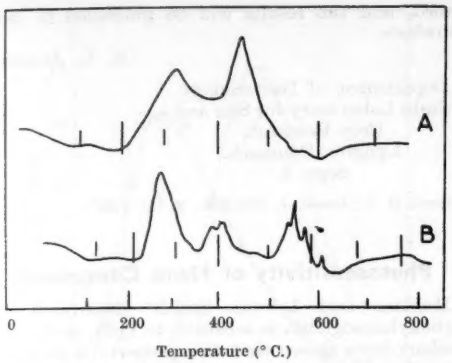

Fig. 2. Complete-combustion differential thermal curves for: *A*, 'humic acid' from *Sphagnum–Eriophorum* peat; *B*, holocellulose from *Sphagnum–Eriophorum* peat

to such differences, variations have been observed in curves for similar fractions separated from peats of different botanical composition.

It has been considered[1] that the area under the exothermic peak in complete combustion may be a measure of the calorific value of coal. The same would be expected to be true of peat, and in addition it may be possible to predict the burning characteristics of different peats from their differential thermal curves.

Systematic application of differential thermal analysis to peats has thus opened up a wide field for further investigation. Several lines are currently being followed up, and it is hoped to publish a more detailed account of the results at a later date.

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Modified Method of Carbon Marking

In the field of experimental embryology, carbon marking has been widely used for tracing the movements of cells[1]. By this method blood carbon particles adhering to the end of a needle are deposited among the cells the migrations of which are to be studied. When experiments are carried out *in ovo*, the needle, before it reaches the embryo, must first pass through the overlying layer of saline, albumen, etc., and the surface-tension effects here, as the needle reaches the surface of this fluid, cause the removal of all the particles not adherent to its very tip. To minimize this effect, it is essential that the needle be held perpendicular, and that a quick stabbing movement be used.

In the method described here, however, these surface-tension effects are eliminated, and hence the needle need not be held perpendicular, and the marking can be carried out slowly and deliberately, and therefore with greater accuracy.

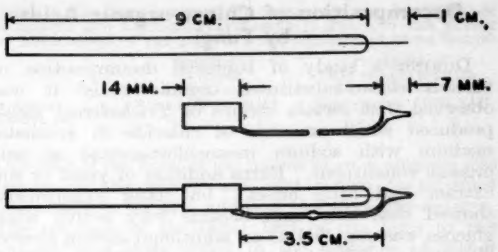

Fig. 1. The components of the carbon-marking device are shown. The dimensions are not in any way critical, but should be varied to suit the size of the individual operator's hand. The handle of the needle is gripped with the forefinger and thumb. The collar is manipulated up or down with the middle finger

The instrument is shown in Fig. 1. It consists of a tungsten needle mounted in a glass handle. A glass capillary tube is fitted over the needle, of a length slightly less than that of the needle itself. To the capillary tube a thin connecting rod is attached. Meanwhile, a collar is made which slides easily up and down on the handle of the needle, and to which a connecting rod is also attached. Both the capillary and the collar are then mounted respectively on the needle and its handle, and the connecting rods brought together and fused with a microburner flame. As the collar slides on the glass handle the capillary moves up and down exposing or covering the tip of the needle.

The instrument is loaded as follows. Blood carbon is placed in a watch glass, and spread out by rubbing with a glass rod. Saline is added. Some of the carbon will float on the surface of the saline, however, but this can be removed by throwing away the saline and refilling. Carbon adhering to the bottom of the watch-glass is picked up under the microscope on the end of the needle; but before withdrawing the instrument from the saline the collar is pushed downwards and the capillary is made to project beyond the tip of the needle so that when the surface film is broken the carbon on the needle remains undisturbed. The embryo is now placed under the microscope and the surface film of the supernatant fluid is broken with the capillary tube still held in the same position, that is, projecting beyond the tip of the needle. The capillary tube is withdrawn slightly exposing the needle tip with its adherent carbon particles. The embryo can now be marked slowly and deliberately in the intended spot.

Care must be taken to ensure that both the needle and the capillary are clean, or the carbon will not go down. Between operations the capillary should be kept wet, otherwise albumen, saline, etc., will clog the instrument. A new capillary is advisable for each operating session.

I wish to express my thanks to Dr. Mary Rawles, under whose direction I worked as a member of the Second International Team in Experimental Embryology, at the Hubrecht Laboratory, Utrecht. I also thank Mr. John Spurbeck for the figure.

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Decomposition of Chloro-organic Acids by Fungi

During a study of bacterial decomposition of various chloro-substituted organic acids[1] it was observed that certain strains of *Trichoderma viride* produced small amounts of chloride in synthetic medium with sodium monochloroacetate as sole organic constituent. Extra addition of yeast or soil extract had little effect; but later experiments showed that the fungi became very active when glucose was supplied as an additional carbon source. Ten strains of *T. viride* were tested in liquid medium containing 0·04 *M* sodium monochloroacetate, 0·2 per cent glucose, 0·05 per cent ammonium sulphate and dipotassium phosphate, 0·02 per cent magnesium sulphate and calcium sulphate, and 0·005 per cent ferrous sulphate. Cultures were incubated at 25° C., and chloride was determined by titration with 0·01 *N* silver nitrate, in the presence of potassium chromate as an indicator. The strains proved to comprise two groups, each of five strains. One of these groups (I) was strongly and the other (II) weakly active towards monochloroacetate. In addition, dichloroacetate was decomposed with moderate vigour, but α-monochloropropionate only feebly (Table 1).

Table 1

Substrate and concentration	Incubation (days)	Per cent ionized Cl: Group I	Group II
Monochloroacetate, 0·04 *M*	7	8–53	0–3
	14	76–100	4–7
Dichloroacetate, 0·02 *M*	7	1–17	0–2
	14	7–28	5–7
Monochloropropionate, 0·04 *M*	7	0–9	0–2
	14	2–17	4–5

The fungi of Group I displayed a similar activity when glucose was replaced by cellulose or xylan.

Sixty-two strains of other fungi, partly collection cultures and partly random soil isolates, were tested against monochloroacetate. The majority (46 strains) had no effect, while ten strains produced chloride in amounts comparable to *T. viride*, Group II. Four strains of *Penicillium roqueforti* (collection cultures) and two of *Clonostachys* sp. (soil isolates) showed an activity approaching that of *T. viride*, Group I. *Clonostachys* sp. also attacked dichloroacetate and α-monochloropropionate, while *P. roqueforti* had very little effect upon these compounds (Table 2).

Table 2

Substrate and concentration	Incubation (days)	Per cent ionized Cl: *P. roqueforti*	*Clonostachys* sp.
Monochloroacetate, 0·04 *M*	7	0–33	5–7
	14	45–76	30–37
Dichloroacetate, 0·02 *M*	7	(0)	3–5
	14	<1–4	16–18
Monochloropropionate, 0·04 *M*	7	(0)	3–4
	14	0–2	13–14

None of the fungi produced chloride from trichloroacetate, α-dichloropropionate, or 2,4-dichlorophenoxyacetate.

Tests with mycelium of *T. viride* grown in submerged culture indicated that formation of a chloride-producing enzyme was induced when mono- or di-chloroacetate was added to the medium. The same enzyme appeared to be responsible for the decomposition of both compounds.

Experiments on the properties of the enzyme and the behaviour of the fungi in soil are being continued, and the results will be published in detail elsewhere.

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Photosensitivity of Hæm Compounds

Haldane and Lorrain Smith[1] discovered that carboxyhæmoglobin is sensitive to light, and several workers have shown that this property is shared by other ferrohæm–carbon monoxide compounds. Until Keilin and Hartree[2] found that the cyanide compounds of ferroperoxidase and myoglobin were light-sensitive, it was generally believed that carbon monoxide compounds were unique in this respect. We have now found that oxyhæmoglobin, nitric oxide hæmoglobin and ethyl isocyanide hæmoglobin are light-sensitive, thus showing that all the known ligands able to combine with ferrohæmoglobin are qualitatively similar.

The compounds were examined by the flash photolysis method[3] the layout of the apparatus following the description of Gibson[4] except that 300*J* were dissipated in each of two borosilicate glass flash tubes and that a Hilger monochromator type *D* 246 was used instead of interference filters. Taking the quantum yield for carboxymyoglobin as 1, the following approximate yields were obtained: oxymyoglobin 0·03, oxyhæmoglobin 0·008, nitric oxide hæmoglobin and nitric oxide myoglobin 0·001, ethyl isocyanide hæmoglobin 0·05. These observations were made at 430 mμ for the hæmoglobin compounds and at 435 mμ for the myoglobin compounds, using a 3-mm. cuvette with 3×10^{-5} *M* hæm pigment, phosphate buffer 0·1 *M*, *p*H 7·1, 1° C.

It should perhaps be pointed out that the photosensitivity of these compounds cannot easily be demonstrated using ordinary light sources. The discharge at present used lasts about 20 μsec., corresponding to an instantaneous rate of work of 3×10^5 kW. In the most favourable circumstances, with a half-time for recombination of oxymyoglobin of 5 msec., a continuous source of about $1{\cdot}2 \times 10^3$ kW. would be needed to maintain half-dissociation if applied in the present apparatus.

For the case of whale oxymyoglobin the absorption spectrum of the product of the photochemical reaction has been determined from the absorption spectrum of the initial solution by measuring the change in optical density produced by the flash at a series of wave-lengths, and subtracting these changes from the initial values. The spectrum so obtained (Fig. 1) corresponded in form to that of reduced hæmoglobin. The recombination reaction has been found to be accurately second-order with rate constant 5×10^6 M^{-1} sec.$^{-1}$ at 1° C. and 12×10^6 at 22° C.

So far we have not been able to cause any ferrihæm compound to dissociate measurably, which, under our conditions, means that the quantum yield must be less than 0·0001. We suggest, therefore, that photosensitivity be regarded, for the present, as a general property of ferrohæm compounds. If further work shows our findings to apply to the hæm enzymes,

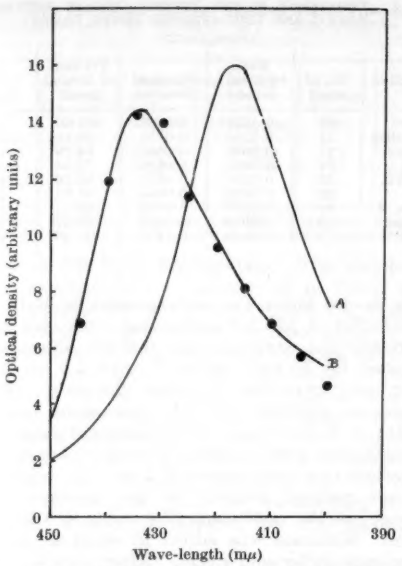

Fig. 1. The continuous lines show the absorption spectra for solutions of reduced myoglobin and oxymyoglobin determined with a spectrophotometer. The points represent the spectrum of the product of flash photolysis of oxymyoglobin. *A*, oxymyoglobin; *B*, myoglobin

flash photolysis may become a useful tool in studies of enzyme action.

We are indebted to the Medical Research Council for grants in aid of this work.

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5-Hydroxytryptamine and Anaphylactic Shock

It is generally accepted that histamine plays an important part in anaphylactic shock. In recent years, attention has been directed to 5-hydroxytryptamine, since this substance, together with histamine, is liberated from the platelets by the antigen–antibody reaction[1]. Further, 5-hydroxytryptamine causes a shock syndrome in guinea pigs which is similar to that caused by anaphylaxis[2]. Although Herxheimer was unable to protect guinea pigs from anaphylactic shock using lysergic acid diethylamide, a potent and specific antagonist of 5-hydroxytryptamine, Pallotta and Ward[3] have observed significant protection using intravenous doses of lysergic acid diethylamide.

We have now attempted to determine, using the Dale–Schultz reaction, whether the substance responsible for the contraction of the sensitized guinea pig and rat uteri in the presence of antigen is histamine or 5-hydroxytryptamine. It was found that the guinea pig uteri (whether from sensitized or normal animals) are at least 1,000 times more sensitive to histamine than they are to 5-hydroxytryptamine, the threshold concentration of histamine being 10^{-8} gm./ml. Guinea pigs were sensitized to horse serum and used for the Dale–Schultz reaction 3–4 weeks later.

Table 1. The Sensitivity of the Guinea Pig and Rat Uteri to Histamine and 5-Hydroxytryptamine (5-HT), and the Effect of Antagonists on the Dale–Schultz Reaction in those Species

	Sensitivity of uterus		Prevention of Dale–Schultz reaction	
Species	Histamine	5-HT	Mepyramine	'BOL 148'
Guinea pig	+	0	+	0
Rat	0	+	0	+

One half of the horn of the uterus of such animals was set up in the organ bath and shown to contract maximally to the first addition of the specific antigen. The reaction of the other half of the horn to the antigen was then tested in the presence of either mepyramine (10^{-6} gm./ml.) or the bromo derivative of lysergic acid diethylamide, 'BOL 148' (10^{-5} gm./ml.). In each of the four tests, mepyramine blocked the reaction, but 'BOL 148' when tested similarly was without effect.

When similar experiments were performed with rat uteri, however, a completely different result was obtained (see Table 1). Uteri of rats (whether from sensitized or normal animals) are at least 1,000 times more sensitive to 5-hydroxytryptamine than they are to histamine, the threshold concentration of the former being 10^{-9} gm./ml. Rats were sensitized by one intraperitoneal injection of either fresh eggwhite alone (2 ml. 50 per cent solution) or horse serum (1 ml.) with *Hæmophilus pertussis* vaccine ($20{,}000 \times 10^{-6}$ organisms, phase I), and used for the Dale–Schultz reaction 12–20 days later. One horn of the uterus of such animals was set up in the organ bath and shown to contract on the first addition of the specific antigen. The reaction of the other horn to the antigen was then tested in the presence of either 'BOL 148' (10^{-6} gm./ml.) or mepyramine (10^{-5} gm./ml.). In each of four tests, 'BOL 148' completely blocked the reaction but mepyramine was without effect when tested similarly, as was also atropine (10^{-7} gm./ml.).

These results illustrate an important species difference in the anaphylactic reaction of the isolated actively sensitized uterus. It appears that, in such a reaction, histamine plays a major part in the guinea pig, whereas in the rat (as in the mouse[4]) 5-hydroxytryptamine plays a more important part than histamine. However, Brocklehurst[5] has recently noted that lysergic acid diethylamide did not antagonize the Dale–Schultz reaction in a passively sensitized rat. Further experiments are now in progress to determine the role of 5-hydroxytryptamine in the general anaphylactic reaction in various species.

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Inhibition of Ascorbic Acid Oxidase by Thiourea

Although ascorbic acid oxidase is regarded as a copper enzyme, thiourea has not been reported as an inhibitor of it. Previous reports, in fact, point out a lack of inhibition of the oxidase by thiourea[1,2], although phenol thiourea has been stated to be inhibitor[3,4]. During a study of the ascorbic acid

oxidase of germinating lettuce seed, thiourea inhibition of the oxidase has been observed. Extracts of lettuce seeds were prepared and tested for ascorbic acid oxidase activity by means of conventional Warburg techniques. Direct titration of ascorbic acid was ruled out as thiourea interferes in the titration.

Extracts of seeds germinated for 48 hr. in thiourea had no activity whatever, while extracts of water-germinated seeds had a high oxygen uptake (408 μl./hr./100 mgm. seeds original weight). Seeds germinated for such a period in thiourea contain 1·2 mgm. thiourea per gm. of dry seeds[5].

In view of the unexpectedness of the results and the known germination stimulatory action of thiourea, its action was further investigated.

The effect of thiourea *in vitro* on the ascorbic acid oxidase activity of extracts of lettuce seeds was therefore tested. As will be seen from Table 1, the inhibition caused by thiourea is very high, of the same order as that caused by cyanide.

Table 1. Inhibition of Ascorbic Acid Oxidase of Lettuce Seed Extracts by Thiourea

Thiourea concentration	Inhibition
$0{\cdot}54 \times 10^{-3}$ *M*	7 per cent
$2{\cdot}8 \times 10^{-3}$ *M*	75 per cent
$1{\cdot}4 \times 10^{-2}$ *M*	100 per cent

The inhibition caused by thiourea *in vivo* could not be removed by thoroughly washing the seeds germinated in the thiourea. *In vitro* inhibition was not reversed by dialysis of extracts to which thiourea had been added.

From these results it can therefore be concluded that thiourea strongly inhibits ascorbic acid oxidase activity *in vitro* and *in vivo*, presumably due to its copper complexing action.

Further details of this work, as well as on the general status of ascorbic acid oxidase activity in lettuce seeds, will be published in the *Bulletin of the Research Council of Israel*, Section D, Botany.

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Metabolism of Pyruvate and α-Ketoglutarate in Virus-infected Mouse Brain

The metabolism of pyruvate and α-ketoglutarate has been studied in normal and virus-infected mouse brain by a modified procedure.

Both these substrates can be metabolized along a number of pathways in a crude brain homogenate; but for the purpose of the present work the conditions were arranged so as to select the step in which the acetyl moiety of the substrate is transferred to co-carboxylase (thiamine pyrophosphate). This is a dehydrogenase step in which artificial electron acceptors may be used[1].

Table 1. Comparison of the Pyruvic Oxidase Activities of Normal and Virus-infected Mouse Brains

Infection	No. of mice	Mean optical density	Standard deviation	Per cent of normal mean	*P*
None	20	0·4732	0·0838	100·00	—
Sabethes	15	0·3753	0·0778	79·31	<0·01
Senger	17	0·3066	0·0685	64·79	<0·001
EMC	18	0·3671	0·0639	77·58	<0·001
GD VII	23	0·3798	0·0677	80·26	<0·001
NV	20	0·3972	0·0984	83·93	0·03
Hæm. A.	26	0·3275	0·0862	69·21	<0·001
Mengo	18	0·3013	0·0633	63·67	<0·001
NWS	17	0·4063	0·1135	85·86	0·03

The mouse brain was homogenized in *M*/15 phosphate buffer of *p*H 8·0 containing 1 per cent gelatin to protect the enzyme, then 0·2-ml. aliquots were incubated for 30 min. at 38° C. with 0·5 ml. gelatin buffer, and pyruvate (or α-ketoglutarate), 10^{-2} *M*; magnesium sulphate, 10^{-3} *M*; potassium malonate, 10^{-3} *M*; 2 : 3 : 5-triphenyltetrazolium chloride, 5 mgm. and methylene blue 1/2,500; all expressed as final concentrations in a total volume of 2 ml. The tetrazolium was not reduced directly in the presence of the enzyme, but the methylene blue acted as a hydrogen carrier. Malonate was added in order to interrupt the tricarboxylic acid cycle. After incubation, the triphenylformazan was taken into solution with glacial acetic acid and extracted into toluene, and the optical density was determined in a spectrophotometer at a wave-length of 495 mμ. In each determination a blank was set up, identical in every respect with the test except for the omission of substrate. Each reading was made against its blank, which represented the unspecific dehydrogenase activity of the tissue.

The following neurotropic viruses have been studied so far: Hæmagogus A, neurotropic vaccinia, the NWS strain of influenza, encephalomyocarditis, GD VII, Mengo, Sabethes and Senger. Details of these viruses are the same as given in a previous publication[2]. The mice were inoculated intracerebrally, then, at the height of the infection, they were killed with ether and the enzyme activity of the brain was assayed.

As will be seen in Table 1, all these virus infections caused a decrease in enyzme activity. When pyruvate was the substrate the fall was quite large, the normal activity being reduced by 15–37 per cent, according to the strain of virus. With α-ketoglutarate, however, a much smaller decrease was observed.

In investigating factors involved in this fall in enzyme activity it was noted that the addition of co-carboxylase would restore the activity of virus-infected brain homogenate almost to that of the normal value. It seems evident, therefore, that the technique used for measuring enzyme activity is a fairly sensitive indicator of the co-carboxylase content of the system; the low enzyme activity found in the virus brains could therefore be a reflexion of a depleted co-carboxylase activity of the tissue. For this experiment, each mouse brain homogenate was set up in duplicate, then to one of these duplicates were added 50 μgm. of co-carboxylase, adjusted to *p*H 8·0, and thiamine sufficient to give a final concentration of 10^{-2} *M*. In place of the phosphate buffer, a 0·1 *M* sodium pyrophosphate–hydrochloric acid buffer was used. The thiamine and sodium pyrophosphate were added in an attempt to reduce the breakdown of co-carboxylase by phosphatases

Table 2. The Effect on Pyruvic Oxidase Activity of Addition of Co-carboxylase to Normal and Virus-infected Brain Preparations

Brain preparation	No. of observations	Mean optical density*		Increase (per cent)	P
		No addition	+ Co-carboxylase		
Normal	9	0·3502	0·4220	17	0·03
Hæm. A infection	9	0·2139	0·3364	37	< 0·001

* A lower enzyme activity was consistently recorded when pyrophosphate buffer was used in place of Sørensen's phosphate buffer.

present in the brain homogenate. The results of a typical experiment are summarized in Table 2.

It is perhaps relevant to note that it has long been recognized that many of the terminal signs of virus encephalitis resemble those of experimental vitamin B_1 deficiency, and although the depletion of co-carboxylase is not so profound in these as has been observed in experimental B_1 deficiency, it seems nevertheless possible that this observed depletion contributes to the terminal signs of virus encephalitis.

Spizizen[3] has recently reported that in phage-infected *E. coli* the pyruvate metabolism falls to zero, but it can be restored by the addition of co-carboxylase.

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Ineffectiveness of Selenium in the Treatment of Nutritional Muscular Dystrophy in the Rabbit

It has been found recently that selenium is effective in the prevention of two experimental syndromes induced by feeding a vitamin E-deficient diet. These are exudative diathesis in the chick (Stokstad, E. L. R., private communication) and necrotic liver degeneration in the rat[1]. Factor III, an unidentified substance in addition to vitamin E and cystine having protective activity against liver necrosis, has been identified as selenium. These reports pose the question whether selenium may have tocopherol-replacing properties with respect to muscular dystrophy, the classical symptom of vitamin E deficiency in the young of most species.

Eight New Zealand white rabbits were fed a tocopherol-deficient diet containing 35·4 per cent 'Cerelose', 37 per cent corn starch, 15 per cent casein, 5 per cent molecular distilled lard, 4 per cent salts, 3 per cent cellulose and a complete vitamin mixture except for vitamin E. Creatine and creatinine in the urine were determined at intervals according to a modification of the procedure of R. S. Hare[2]. After six weeks on the depletion diet the animals exhibited the well-known symptoms of muscular dystrophy and an increase in the creatine : creatinine ratio to 2–4 : 1. Six rabbits were treated intramuscularly with either 20 μgm. or 100 μgm. selenium per day as sodium selenite. Administration of this compound for periods up to 17 days elicited no response in the symptoms of dystrophy or in the level of creatine excretion. Administration of DL-α-tocopheryl acetate orally at a rate of 15 mgm. per day to two controls induced a remission of symptoms and creatinuria in about five days.

These results indicate that nutritional muscular dystrophy is of more specific etiology than exudative diathesis or liver necrosis.

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Induction of Mouse Leukæmia with Purified Nucleic Acid Preparations

Recent studies by Gross[1] and others[2,3] have shown that leukæmia with immunogenetic characteristics of the recipient strain can be induced in certain low-leukæmia-incidence strains of mice by injecting into newborn animals cell-free extracts of tissues of certain high-leukæmia strains. Although the active leukæmogenic agent has been referred to as a virus, direct evidence on this point has been lacking. At present it can be said only that the agent is filtrable and thermolabile, and is transmitted in certain families of mice from one generation to another directly through the embryos. Under certain poorly defined conditions, cell-free extracts of leukæmic organs may also produce parotid gland tumours, sarcomas and perhaps other neoplasms, indicating that the active agent is either multipotent or that extracts contain several oncogenic agents.

It is evident, therefore, that while this phenomenon could be due to the transfer of discrete infective virus particles (here defining 'virus' in conventional terms which exclude the so-called provirus), it could also be visualized either as a process analogous to transduction by an agent resembling lysogenic bacteriophage (wherein the active nucleic acid would reside within a more complex deoxyribonuclease-resistant particle) or to bacterial transformation (wherein the active agent is free deoxyribonucleic acid).

The present report describes a series of experiments in which the incidence of leukæmia was apparently increased in a hybrid strain by injection into newborn mice of purified nucleic acid prepared from the lymphoid tissues of a high-leukæmia donor strain.

In a preliminary experiment, cell-free extracts were tested according to the method of Gross. 'Selas'-filtered extracts of the leukæmic tissues of *AKR* mice were injected into newborn mice of two low-leukæmia strains, *C3H$_f$/Gs* and *C57BR/cd*, and into *C3H$_f$* (female) × *AKR* (male) F_1 hybrids. The results shown in Table 1 essentially confirm the basic observations of Gross.

In the next experiment (Table 2), mice were injected under similar conditions with saline suspensions of deoxyribonucleic acid and ribonucleic acid that had been isolated from non-leukæmic and leukæmic organs of *AKR* mice. The nucleic acids were isolated by a general method reported to yield active transforming deoxyribonucleic acid from pneumococci[4] and to disrupt tobacco mosaic virus[5] and various *E. coli* bacteriophages[6]. Frozen, freshly collected lymphoid tissues (spleens and lymph nodes) were homogenized in 0·01 *M* versene at *p*H 7 and treated with 15 per cent sodium dodecyl sulphate

Table 1. Incidence of Leukæmia in Three Strains of Mice receiving Cell-free ('Selas' Filtered) Extracts of Leukæmic *AKR* Mouse Tissues in the Newborn Period

Strain		Total animals	Leukæmia	Mean age of leukæmia development
C3Hf/Gs	Injected	36	10 (27·8%)	8·7 months
	Controls	83	0	—
C57BR/cd	Injected	47	7 (14·9%)	10·3 months
	Controls	120	4 (3·3%)	18·5 months
C3Hf × *AKR* F_1 Hybrid	Injected	51	11 (21·6%)	9·5 months
	Controls	65	5 (7·7%)	9·4 months

at *p*H 7·5 at 25° for 18 hr. After removal of sodium dodecyl sulphate at 0° as the insoluble potassium salt, the extract was deproteinized in the cold at *p*H 4·3 in the presence of 10 per cent sodium xylene sulphonate. After neutralization, the nucleic acids were precipitated by the addition of an equal volume of 98 per cent isopropyl alcohol. The isolated nucleic acids were dissolved in a minimum amount of water and sodium xylene sulphonate was added to a concentration of 30 per cent at *p*H 7·5 (to dissociate any residual nucleoprotein). After the addition of two volumes of water, the deproteinization was repeated at *p*H 4·3 and 0°. The nucleic acids were re-precipitated with isopropyl alcohol, isolated, redissolved and fractionally precipitated with 0·7 vol. isopropyl alcohol in the presence of 0·3 *M* sodium acetate and 0·01 *M* versene. The resulting precipitate of deoxyribonucleic acid and ribonucleic acid (in almost quantitative yield) was finally washed with ethyl alcohol and dissolved to a concentration of 0·1 per cent in sterile 0·85 per cent sodium chloride and stored frozen until used. 0·1 ml. of this material was injected into newborn mice.

As shown in Table 2, seventeen *C3Hf/Gs* and forty-one *C57BR/cd* animals were injected with the nucleic acid preparations from leukæmic *AKR* tissues. No leukæmias developed in these animals. Of the twenty-three *C3Hf* × *AKR* F_1 hybrid animals injected with non-leukæmic *AKR* deoxyribonucleic acid – ribonucleic acid, six developed leukæmia. Five of eight animals receiving deoxyribonucleic acid – ribonucleic acid from leukæmic *AKR* organs developed leukæmia. Five spontaneous leukæmias occurred in two litters out of fourteen non-injected control litters (sixty-five animals). All these results are statistically significant at 5 per cent level with the χ^2 test.

Table 2. Incidence of Leukæmia in Three Strains of Mice receiving Nucleic Acid Preparations (DNA–RNA) of *AKR* Mouse Tissues in the Newborn Period

Strain		Total animals	Leukæmia	Mean age of leukæmia development
C3Hf/Gs	Injected with leukæmic *AKR* DNA–RNA	17	0	—
	Controls	83	0	—
C57BR/cd	Injected with leukæmic *AKR* DNA–RNA	41	0	—
	Controls	120	4 (3·3%)	18·5 months
C3Hf × *AKR* F_1 hybrid	Injected with non-leukæmic *AKR* DNA–RNA	23	6	11·4 months
	Injected with leukæmic *AKR* DNA–RNA	8	5 (35·4%)	11·3 months
	Controls	65	5 (7·7%)	9·4 months

It is emphasized that the deoxyribonucleic acid – ribonucleic acid from the non-leukæmic *AKR* mice, as well as that from the leukæmic animals of the same strain, was apparently active in producing an incidence of leukæmia in the hybrids comparable to that of cell-free extract injected animals.

Two of the leukæmias developing in the deoxyribonucleic acid – ribonucleic acid-injected group and one in the non-leukæmic deoxyribonucleic acid – ribonucleic acid group were transferred by cells to F_1 hybrid animals and to animals of the two parent strains. The tumour grew progressively, resulting in death of the hybrid recipients, but did not grow in *AKR* or *C3H* animals.

These preliminary results in hybrid animals suggest that free nucleic acid is leukæmogenic, although the possibility is not ruled out that a virus or provirus is, in fact, the active agent in cell-free extracts, and that our preparations contain active virus nucleic acid. It is unlikely, however, that intact active virus could survive the nucleic acid isolation procedure. Experiments are now in progress to test the activity of deoxyribonucleic acid – ribonucleic acid obtained from the tissues of low-leukæmia mice and from other species and to determine the effect on active cell-free extracts of deoxyribonuclease and ribonuclease. A full report of these investigations will be published separately.

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Sensitization by Œstradiol to the Production of Experimental Nephrocalcinosis

Earlier experiments showed that excessive oral administration of mono- or dibasic-phosphates produces nephrocalcinosis in the rat, and that these renal lesions are aggravated by mineralocorticoids, such as deoxycorticosterone[1-3]. Recent experiments revealed that, under similar experimental conditions, the nephrocalcinosis produced by oral administration of acid sodium phosphate is not aggravated by methyltestosterone, progesterone, corticosterone, Δ^1-cortisol acetate, or Δ^1-cortisone acetate, but curiously, œstradiol proved to be even more effective in this respect than deoxycorticosterone. It has long been known that folliculoid or 'œstrogenic' hormones exert a pronounced effect on calcium metabolism in birds, presumably because in the avian species the production of calcified egg shells is closely related to the action of sex hormones. In mammals, on the other hand, folliculoids do not exert any comparably pronounced effect upon calcium

Table 1

Group	Œstradiol	NaH_2PO_4 (per cent)	Nephrocalcinosis (Scale 0–3)	Mortality (per cent)	Duration of experiment (days)
I	none	10	0·6	0	12
II	500 μgm.	10	2·2	40	12
III	none	10	0·2	0	15
IV	500 μgm.	10	2·3	10	15
V	none	20	0·2	0	5
VI	500 μgm.	20	*	100	5
VII	none	30	1·3	0	9
VIII	500 μgm.	30	3·0	80	9

* All animals in this group died within first three days, hence there was insufficient time for the development of marked nephrocalcinosis; besides, the intensity of calcification could not be compared with that of the corresponding controls (Group V), since the latter were killed on the fifth day.

metabolism, and, therefore, the production of intense nephrocalcinosis by œstradiol (when given in combination with phosphates) was made the subject of a special study.

Eighty female Sprague–Dawley rats with an average body-weight of 100 gm. (range: 95–111 gm.) were subdivided into eight equal groups and treated as indicated in Table 1.

Œstradiol was administered in the form of microcrystals at the daily dose of 500 μgm. in 0·2 ml. of water, subcutaneously. Aqueous solutions of acid sodium phosphate were given, by stomach tube, in two daily doses of 2 ml.

The degree of nephrocalcinosis was estimated both macroscopically (judged by the appearance of whitish spots on the outer and cut surface of the kidneys) and microscopically (after staining neutral-formalin-fixed, paraffin-embedded sections with Kossa's silver nitrate technique). The intensity of the calcification was gauged in terms of an arbitrary scale of 0–3, the means of the readings in each group being listed in Table 1.

It is evident from Table 1 that, under our experimental conditions, the 10 per cent acid sodium phosphate solution in itself caused only traces of nephrocalcinosis, but resulted in marked renal calcification when given conjointly with œstradiol. Otherwise untreated rats tolerated even 20 or 30 per cent acid sodium phosphate under these conditions, while in animals simultaneously treated with œstradiol, these concentrated phosphate solutions resulted in a high mortality and an aggravation of the nephrocalcinosis.

Since œstradiol is completely devoid of mineralocorticoid, and deoxycorticosterone of folliculoid actions, the enhancement of nephrocalcinosis appears to be an 'independent steroid hormone action', in the sense in which this term has been defined[4].

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Fluoride Removal by Powdered Dental Enamel from Solutions of Stannous or of Sodium Fluoride

In 1955, Hatton, Nebergall and Muhler[1] described an experiment in which powdered enamel samples were shaken in dilute solutions of stannous fluoride or of sodium fluoride that initially contained equivalent concentrations of fluoride. Much more fluoride was removed (presumably taken up by the enamel) from the stannous fluoride solution; for example, when the final concentrations of fluoride were 17 μgm./ml., 7–8 times as much fluoride was removed from the stannous as from the sodium fluoride solution. Hatton *et al.* suggested that the greater initial acidity of the stannous fluoride solutions may have been in part responsible[2]. Another important *p*H effect was overlooked by Hatton *et al.*, namely, shaking with powdered enamel increased the *p*H of the solutions, markedly for stannous fluoride and detectably for sodium fluoride. Stannous fluoride solutions are not stable when the *p*H increases and even at acid *p*H's on standing. Nebergall, Muhler and Day[3] described the opalescence, "probably stannous hydroxide" (contained less than 0·01 per cent fluorine), which developed and was ultimately precipitated from a solution of *p*H 2·38. We found that by increasing the *p*H of stannous fluoride solutions in the absence of enamel, precipitates were formed which contained larger percentages of fluoride ($\geqslant$ 0·01 per cent fluoride) that might account at least in part for the greater amount of fluoride removed from stannous fluoride solutions. Amorphous precipitates were seen microscopically along with the centrifuged enamel particles when powdered enamel was shaken with stannous fluoride solutions.

Solutions of stannous fluoride (initial *p*H, 3·5) were prepared according to Nebergall[3] containing approximately 40 p.p.m. fluorine. The *p*H was adjusted using a dilute sodium hydroxide solution to approximately 4·5; the solution was protected from air and shaken mechanically for 24 hr. Following centrifugation an aliquot of the supernatant solution was taken for fluoride analysis. The precipitate was resuspended, the *p*H adjusted to approximately 5·5 and the mixture stirred for another day. This process with increments of *p*H was repeated daily for eight days; the *p*H on the final day was brought to 8·6 before the final 24-hr. agitation. Fluoride analyses of the supernatant solution showed that as the *p*H

Table 1. Overall Amounts of Fluorine (μgm.) in 50 ml. of Stannous or Sodium Fluoride Solutions Before and After Shaking with 1 gm. of Enamel. Estimates of Fluorine Removed from Solution by Enamel and by Precipitation

Initial fluorine (*a*)	Stannous fluoride solution			Sodium fluoride solution. Fluorine removed by enamel (*d*)
	Hatton *et al.* (*b*)	Present series (*c*)	Estimate of fluorine removed by enamel only (*b*–*c*)	
100	50	0	50	52
250	150	135	15	65
500	300	175	125	145
750	475	275	200	175
1,000	600	375	225	225
1,250	750	475	275	225
1,500	900	575	325	250
1,750	1,050	700	350	250
2,000	1,200	750	450	250

a, Interpolated values, see text; *b*, fluorine removed from solution shaken with enamel (Hatton *et al.*, ref. 1); *c*, fluorine removed from solution by alkalinization to *p*H 6·5; *d*, Hatton *et al.* (ref. 1).

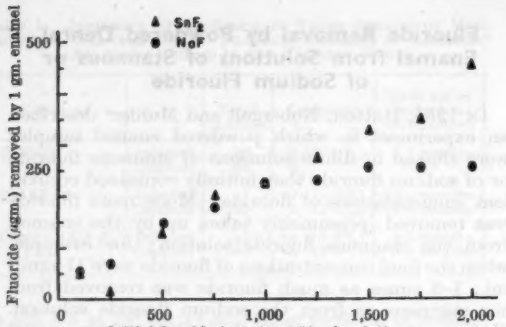

Fig. 1. Interpolated data on fluoride removed by powdered enamel from solutions of stannous fluoride or of sodium fluoride. Initial concentrations ranged from 2 to 40 p.p.m. fluorine, expressed (abscissal) as total μgm. fluorine per 50 ml. of solution

was raised to 6·5, more and more fluoride was removed from solution. At higher *p*H's fluoride redissolved. From a graph of fluoride concentrations in the supernatant solution before and after each increment in *p*H, the μgm. of fluorine removed (column *c*, Table 1) could be read by interpolation at an arbitrarily chosen series of initial concentrations of fluorine (column *a*). From a similar graph of the results of Hatton *et al.* on stannous fluoride solutions shaken with enamel, the μgm. of fluoride removed were read at the same interpolated initial concentrations (column *b*). We propose that these are the over-all amounts removed: (1) by fixation on enamel, plus (2) that in the precipitated amorphous material. Differences (that is, the fluorine fixed by enamel (columns *b*–*c*)) are plotted in Fig. 1 (triangles); the amounts of fluorine removed from sodium fluoride solutions (column *d*) are included (circles). With the possible exception of the points at the higher concentrations (extreme right), no discrimination can be drawn between results from stannous fluoride and sodium fluoride solutions. At the higher concentrations more fluoride may have been taken from the stannous fluoride solutions; however, the differences are not great and the higher initial acidity may be responsible[3].

In confirmation, powdered enamel samples were shaken with solutions containing about 30 p.p.m. fluorine as stannous fluoride (initial *p*H 3·5) or as sodium fluoride (initial *p*H 3·0) for periods of 6 hr. Fluoride analyses of supernatant solutions following centrifugation showed again that more fluorine was removed from the stannous fluoride than from the sodium fluoride solution. The particles were resuspended in distilled water and then, by means of a coarse filter and washing with distilled water, the enamel particles were separated mechanically from the amorphous precipitate that had formed in the stannous fluoride solution. We could account for the extra fluoride initially removed from the stannous fluoride solution by analyses of the washings containing the amorphous precipitate.

In summary, approximately equivalent amounts of fluoride were removed by powdered enamel from solutions of the same initial fluorine concentrations of stannous fluoride or of sodium fluoride. An amorphous precipitate separating from stannous fluoride solutions shaken with powdered enamel contained additional fluoride.

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Denaturation of Fish Proteins

Reporting on the influence of freezing-rate on the denaturation of cold-stored fish, Love[1] states that organoleptically determined toughness of cod, stored at − 30° C., does not always involve decreased protein solubility.

In my experiments, using Dyer's[2] extraction method with 5 per cent sodium chloride solutions adjusted to *p*H between 7·0 and 7·5, the content of soluble nitrogen of quick-frozen cod samples, stored at different temperatures, determined by micro-Kjeldahl determination, was compared at regular intervals with the organoleptically determined toughness after boiling.

In the samples stored at − 10° C. a close relation was always found between increase of toughness after boiling and decrease of the ratio soluble nitrogen/total nitrogen, as reported by Dyer[3]. However, in samples stored at − 20° C. and − 30° C. this correlation was absent. Typical curves for changes in toughness and nitrogen solubility are given in Fig. 1. All samples had been frozen in an airblast-freezer, the time necessary for cooling the centre of the fish from 0° C. down to − 5° C. being about 20 min. The rather low soluble-nitrogen content just after freezing may be explained by the results of Ironside and Love[4], who found low values for big fish, especially when the samples contained mycommata tissue, such being the case with our samples. The rather low initial consistency values reflect the toughness of frozen fish, which is always greater than that of unfrozen fish.

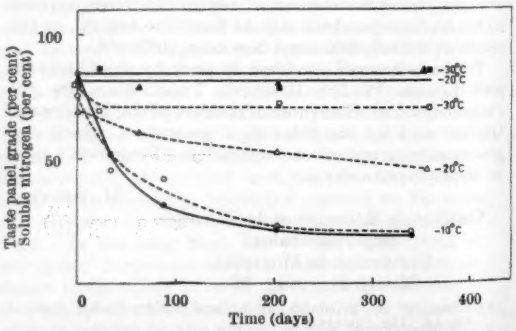

Fig. 1. Taste panel grades for consistency (dotted lines), expressed as per cent of maximum grade, and soluble nitrogen (solid lines), expressed as per cent of total nitrogen, in frozen cod, stored at different temperatures

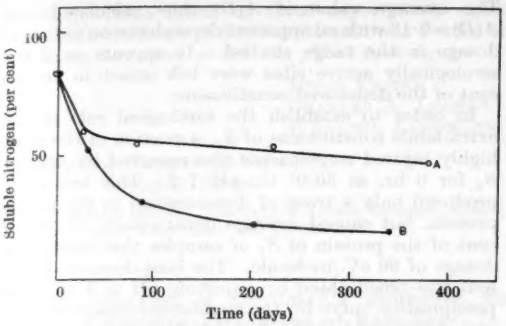

Fig. 2. Decrease of soluble nitrogen, expressed as per cent of total nitrogen, in cod, frozen in fresh condition (*B*) and in spoiled condition (*A*) and stored at − 10° C.

These results indicate that in practice the determination of soluble nitrogen (or protein) expressed as percentage of the total nitrogen, cannot be used as an objective standard for the toughness of cold-stored fish, because substantial toughness need not be related with a considerable decrease in the soluble-nitrogen content.

Experiments with cod, quick-frozen at different degrees of freshness and stored at − 10° C., proved that in samples frozen in fresh condition, protein denaturation is quicker and proceeds down to a lower level of soluble nitrogen than in samples frozen in a condition of rather advanced spoilage (Fig. 2). This indicates that the action of bacteria and enzymes decomposes the proteins to such a degree that they are less liable to denaturation.

Hitherto, protein denaturation in frozen white fish has always been considered to be connected with toughness[3,5]. Therefore, it can be understood that this denaturation has been stated to be fundamentally different from protein denaturation caused by heating. Usually the denaturation phenomena in frozen fish are seen as a result of the action on the soluble proteins of concentrated salt solutions, originating from the liquid in and around the cells when pure water freezes out[5,6].

Some observations of denaturation of meat proteins at temperatures above the freezing point are known[7,8]. In fresh fish we have never been able to demonstrate protein denaturation at temperatures from − 1 to + 24° C. However, this does not prove that at these temperatures fish proteins could not be liable to heat denaturation at all. It might be possible that the rate at which the proteins are broken down by the action of bacteria and enzymes is so high that no denaturation at all can be demonstrated. We tried to prove this hypothesis by storing sterile native fish proteins at temperatures above the freezing point.

In a few samples, cod tissue sterilized by γ-irradiation in hermetically sealed cans and afterwards stored at respectively +10° and + 24° C., we were able to demonstrate protein denaturation. To get sterile samples, a radiation dose of $0{\cdot}5 \times 10^6$ rad was necessary. Due to this irradiation the soluble-nitrogen content decreased from 88 to 47 per cent. During storage at 10° C. for 13 days the soluble-nitrogen content in two samples decreased further to 26 and 27 per cent respectively. In three samples stored at 24° C. for 16 days the soluble-nitrogen content decreased to 22, 23 and 24 per cent respectively. At both temperatures, samples were taken only once, and therefore these results do not give any indication about the velocity of the denaturation. All that can be said in this respect is that the samples stored at 10° C. for 13 days had not yet reached their minimum content of soluble nitrogen by then. After boiling, the soluble-nitrogen content in an identical sample that had not been irradiated was 24 per cent. The minimum value found in non-irradiated samples stored for a very long time at − 10° C. is about 20 per cent.

The experiments described, so far as we are dealing with irradiated samples, have the disadvantage that by the irradiation itself, much protein is denatured and it might be possible that the denaturation during storage has been induced by the irradiation.

Experiments with aseptically dissected sterile fish tissue are in progress.

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Role of Structural Degradation in the Loss of Serological Activity of Ovalbumin irradiated with Gamma-Rays

Although it has long been known that ionizing radiations cause denaturation of proteins, as defined by loss of solubility at the isoelectric point, it is yet not known to what extent denaturation is correlated with the radiation loss of biological function. In addition to the denatured constituents, irradiated proteins such as ovalbumin and hæmoglobin contain a broad band of structurally injured molecules, characterized by their increased thermal lability with respect to denaturation[1]. Experiments were performed to establish the part played by these various kinds of structural degradation reactions in the loss of serological activity of ovalbumin irradiated with γ-rays.

Ovalbumin was irradiated in lyophilized form (8–10 per cent water) in vacuum at 0° C. in a homogeneous γ-ray field of $1{\cdot}5 \times 10^6$ r./h. and afterwards completely dissolved in aerated water at *p*H 7–9 sodium hydroxide, 0° C. Proteins were characterized serologically by measuring at 0° C., *p*H 7·2, the precipitations formed from the reaction of various quantities of antigen with a fixed quantity of anti-native rabbit serum. The entire range of combining proportions was studied; however, the precipitin curves in Fig. 1 represent only the precipitations formed near the peaks, that is, from the region of slight antigen excess to the region of slight antiserum excess.

For ovalbumin preparations irradiated so as to absorb up to 100 electron volts per protein molecule, the effect of irradiation is to shift the precipitin curves parallel to the abscissa towards the

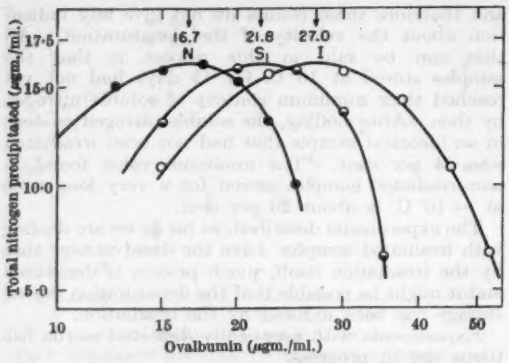

Fig. 1. Reaction of anti-native ovalbumin rabbit serum with native ovalbumin (N); irradiated ovalbumin—dose 60 eV./molecule γ-rays (I); and residual protein obtained after removing the irradiation-denatured fraction from $I(S_1)$. The arrows indicate the position of the peaks on the abscissa

side of higher antigen concentrations, with no systematic change in the form of the curves (Fig. 1), so far as can be established with our present techniques. An irradiated ovalbumin system behaves thus essentially as a mixture of protein molecules which have either completely retained or completely lost their original serological activity. This suggests that the essential underlying mechanism involves structural degradation rather than localized chemical changes in the protein molecule. The fraction of apparently serologically intact protein molecules—termed the serological activity of the system—was obtained as the ratio of the abscissæ of the peaks of the precipitin curves for the native and the irradiated system.

It would be easiest to understand these observations if the loss of serological activity resulted wholly from denaturation; but this is not the case. The denatured protein was obtained by precipitating it at 0° C., pH 4·85, the approximate isoelectric point of both the radiation altered and native protein species[1]. Curves representing serological activity and non-denatured protein as functions of radiation dosage are shown in Fig. 2. The former curve lies considerably below the latter. Thus, even if the radiation-denatured protein were serologically completely inactive, as further study showed it not to be, it would account for only a fraction of the loss of serological activity. The G values for initial loss of serological activity and initial denaturation were respectively 1·25 and 0·64.

That the loss in serological activity was too large to be accounted for by denaturation was shown also by precipitating the denatured constituents (D) from the irradiated system (I) and measuring the serological activity of the supernatant (S_1). The precipitation curve for S_1 lay a considerable distance to the right of the precipitation curve for the native ovalbumin (N) (Fig. 1).

On the basic assumption of the all-or-none mechanism, the serological activity $A(D)$ of the denatured fraction may be calculated from:

$$A(I)=[D]\cdot A(D)+(1-[D])\cdot A(S_1) \qquad (1)$$

where $A(I)$ and $A(S_1)$ represent the serological activities of I and S_1 respectively and $[D]$ is the fraction of denatured protein in I. From this equation, $A(D)$ can be calculated from observed quantities. The average value of $A(D)$ thus calculated was $A(D)=0{\cdot}16$ with no apparent dependence on radiation dosage in the range studied. It appears as if the serologically active sites were left intact in 16 per cent of the denatured constituents.

In order to establish the serological role of the extra-labile constituents of S_1, a portion of the most highly injured constituents was removed by heating S_1 for 6 hr. at 50·0° C., pH 7·2. This treatment produced only a trace of denaturation in the native protein, but caused average denaturation of 38 per cent of the protein of S_1 of samples that received a dosage of 60 eV./molecule. The heat-denatured protein was precipitated by adjusting pH to 4·85. The precipitation curve for the neutralized supernatant S_2 was determined. The form of this curve was the same as that of the native ovalbumin, but its position in the co-ordinate system relative to that of S_1 was shifted toward, but was still slightly to the right of, the native.

Further differential removal of the extra-labile constituents was affected by heating S_2 at 62·0° C., pH 7·2 and precipitating at pH 4·85. Among preparations of ovalbumin that had been prepared in the dosage range 30–60 eV./molecule, the serological activity of the supernatants was experimentally indistinguishable from that of the native ovalbumin after four hours of heating.

Control experiments on the native protein showed that heating under the conditions used was without influence on the serological activity of the non-denatured portion of the system. If we assume that this is true also for the irradiated systems, our observations prove that the loss of serological activity, after removal of the denatured protein, is mainly associated with the thermolabile constituents, and particularly those of low stability. By using an analogue of equation (1), we can calculate the serological activity of the fractions removed during the various stages of the heat treatments used. The

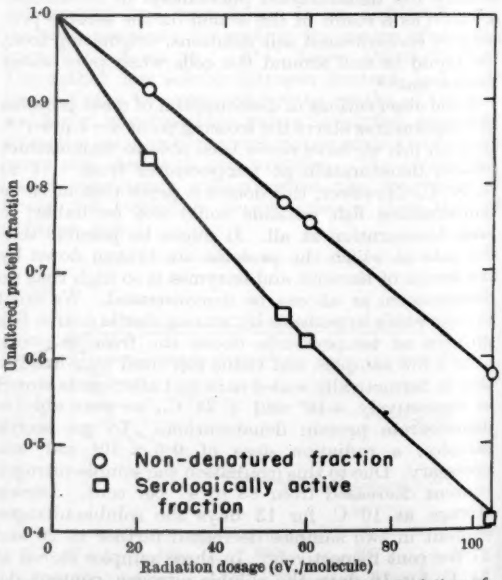

Fig. 2. Effect of radiation dosage on properties of solutions of ovalbumin irradiated with γ-rays. Each point represents the average of values obtained from three experiments

average value found in three experiments carried out with a dosage of 60 eV./molecule was 0·4 for the fraction removed at 50° C., *p*H 7·2, 6 hr.

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Transaminases of *Leishmania donovani*, the Causative Organism of Kala-azar

WHILE making a systematic investigation into the role of individual amino-acids on the nutritional requirements of *Leishmania donovani*, a protozoal parasite causing the disease kala-azar, strong transaminase activities were detected in the cell-free extracts of this organism. *L. donovani*, strain 81, cultured on Ray's medium[1] at 22–24° C. was used for this investigation. After growth for three days on this medium the organism was scraped from the surface of the agar, washed once with isotonic saline, and then ground with sand, with gradual additions of distilled water. The crushed suspension was centrifuged at 2,500 r.p.m. for 10 min. and the supernate was used as the crude enzyme extract.

Transaminase activities were demonstrated by incubating the enzyme extract with either α-ketoglutarate or pyruvate and the corresponding NH_2-group donors like amino-acids, amino-acid amide, glucosamine, adenine, etc., when formation of glutamate or alanine was noted. For the identification and approximate quantitative determination of the amino-acids in the reaction products, paper chromatography by the ascending method was used. The incubation mixture for the assay of the enzyme activity consisted of 1 ml. of the crude extract (containing nearly 1 mgm. protein N/ml.), 1 ml. 0·13 *M* amino-acids or other amino donors, 0·5 ml. 0·25 *M* keto-acid, 0·5 ml. 0·05 *M* phosphate buffer (*p*H 7·8) in a total volume of 5 ml. The temperature of incubation was maintained at 32° C. Amino-acids used were all of DL-varieties, unless otherwise mentioned.

The presence of both α-ketoglutaric and pyruvic transaminase activities with a number of amino-acids was demonstrated. With α-ketoglutarate, the highest transaminase activities were observed with aspartic acid, histidine, methionine, lysine, cysteine, both α- and β-alanines, phenylalanine, tyrosine and tryptophan, lower activity with valine, ornithine, arginine, proline, threonine, nor-valine, nor-leucine, taurine, serine and glycine, whereas very feeble or negligible transamination occurred in the presence of hydroxyproline. With pyruvate, on the other hand, the highest transaminase activities were found with arginine, histidine, methionine, ornithine, phenylalanine and tyrosine; lower activities with lysine, β-alanine, typtophan, glutamic acid, serine, *iso*leucine, leucine, proline and γ-amino butyric acid, while very low activities were found with cysteine, aspartic acid, threonine and hydroxyproline. Among the amino-acid amide transaminases both glutamine and asparagine transaminase systems were very strong in the cell-free extracts of this organism. The presence of such active glutamine-keto acid and asparagine-keto acid transaminases, which occur also in rat liver and kidney[2], suggests that both glutamine and asparagine might play a significant part in the amino-acid metabolism of this protozoal organism. Using glucosamine, the transaminase activity with either α-ketoglutarate or pyruvate was found to be relatively lower. Among the various purines and pyrimidines tried, only adenine, guanine and cytosine could transaminate with pyruvate but not with α-ketoglutarate in this extract. This suggests a new mechanism of formation and interconversion of purines and pyrimidines in this protozoal organism. A similar observation has also been reported in *E. coli* preparations[3].

Repeated dialysis for 96 hr. in ice-cold temperature, charcoal treatment or ageing at room temperature for 2–3 hr., failed to reveal any requirement for pyridoxal phosphate or pyridoxamine phosphate. This failure may also be due to the difficulty of obtaining enzyme preparations free from pyridoxal phosphate-like co-factors.

Among the various inhibitors tried (used at 10^{-3} *M* concentrations) potassium cyanide, hydroxylamine, 2,4-dinitrophenyl hydrazine, mercuric chloride, silver nitrate, *p*-chloromercuric benzoate were found to have the most striking inhibitory effects on this system. The following inhibitors or compounds were tried and found to be inactive: iodoacetate, azide, isoniazid, urea stibamine, 8-hydroxyquinoline and sulphone.

Detailed studies dealing with the kinetics and other properties of this protozoal enzyme system will be reported in a separate communication elsewhere.

Our thanks are due to Dr. J. C. Ray and Prof. B. C. Guha for their interest in this work.

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An Effect of Hexylresorcinol on Bacterial Aerosols

DURING the course of some investigations into the effects of volatile germicides on the viability of bacterial aerosols, we have encountered a phenomenon which appears to have escaped the notice of other workers in this field, and which not only accounts for contradictions in some existing experimental results, but also suggests that in certain circumstances substances such as hexylresorcinol may be of considerably greater value as barriers to cross-infections than has been supposed hitherto.

When spraying bacterial aerosols into atmospheres containing small concentrations of hexylresorcinol vapour (0·1 μgm./l.), we observed that the initial recovery of the organisms immediately after spraying was frequently very much less than could be accounted for by the often rather slow killing-rate computed from a series of subsequent samples. Control experiments show that this mortality was not attributable to any factor other than the presence of the bacteri-

cide. This suggested that the organisms contained in an evaporating droplet were rendered non-viable more rapidly than those that had reached equilibrium with their surroundings, possibly owing to the absorption of a relatively large quantity of hexylresorcinol when the droplet surface area was at its maximum, with subsequent concentration on evaporation.

If the above supposition is correct, then this 'initial kill' phenomenon should not occur when the experimental procedure is reversed and hexylresorcinol vapour introduced into an already established bacterial aerosol. This is found to be so. Further confirmatory evidence has been obtained by dissolving hexylresorcinol in bacterial suspensions in quantities insufficient to affect the viability of the organisms, and atomizing the product into clean air, whereupon an immediate and very considerable reduction was observed.

We have encountered the phenomenon with both Gram-negative and Gram-positive organisms, though in some cases it appears to be inhibited by certain suspending fluids. Experimental results are being published elsewhere.

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A Biochemical Lesion in Congenital, Non-obstructive, Non-hæmolytic Jaundice

Congenital, non-obstructive, non-hæmolytic jaundice is a syndrome characterized by marked elevation of 'indirect-reacting' (free) bilirubin in the blood[1]. Recent studies have shown that bilirubin forms a polar glucuronide which is readily excreted in the bile[1]. The synthesis of bilirubin glucuronide has been found to be catalysed by an enzyme system in the microsomes of the liver that transfers glucuronic acid from uridine diphosphate glucuronic acid to a suitable aglycone[2]. We wish to describe experiments showing that the accumulation of free bilirubin in this syndrome is the result of a defect in the glucuronide-forming mechanism.

The availability of a mutant strain of Wistar rats exhibiting congenital jaundice, previously described by Malloy and Loewenstein (ref. 1,*a*), made it possible to examine the biochemical lesion involved in this type of jaundice. Studies in our laboratory have shown that non-jaundiced animals of this mutant strain have no detectable bilirubin in the serum, and large amounts of bilirubin glucuronide (as determined by paper chromatography) in the bile. On the other hand, in jaundiced animals, free bilirubin is high in the serum, but no bilirubin glucuronide is present in the serum, urine or bile. The biliary excretory function is not impaired, as shown by rapid excretion of injected bromsulphalein, cholografin and bilirubin glucuronide. These observations suggest a defect in the conversion of bilirubin to its glucuronide.

After the oral administration of *o*-amino-benzoic acid, a compound known to form a glucuronide *in vivo*, it was found that jaundiced rats excreted in the urine one-fourth the amount of glucuronide as compared to non-jaundiced controls. *In vitro* synthesis of glucuronide was then examined by incubating *o*-aminophenol and uridine diphosphate glucuronic acid with liver microsomes. The results shown in Table 1 indicate that in jaundiced rats the enzymatic formation of *o*-aminophenol glucuronide was much less than that found in non-jaundiced litter mates ($P < 0.001$), but not entirely absent. The possibility that inhibitory factors may be present was studied by measuring *o*-aminophenol glucuronide formation in an incubation mixture containing liver microsomes from jaundiced and control rats. No reduction in enzymatic activity of the microsomes from non-jaundiced rats was observed. These results differ from a recent report stating that in jaundiced rats "glucuronyl transferase activity is absent or inhibited"[3]. The ability to form uridine diphosphate glucuronic acid was found to be the same in both types of rats (Table 1).

Table 1. Enzymatic Synthesis of *o*-Aminophenol Glucuronide and Uridine Diphosphate Glucuronic Acid in Jaundiced and Non-jaundiced Rats

o-Aminophenol glucuronide formation (measured by the procedure of Levvy and Storey, ref. 4) was determined after incubating 0·2 μmole *o*-aminophenol (in 0·01 *M* ascorbic acid) for 30 min. at 37° C. with washed microsomes obtained from 1 gm. of male rat liver, 25 μmoles magnesium chloride, 0·1 ml. *tris* (hydroxymethyl) amino-methane buffer, *p*H 8·0, 0·3 μmole uridine diphosphate glucuronic acid (prepared enzymatically from uridine diphosphate glucose with its dehydrogenase and diphosphopyridine nucleotide, ref. 5) and water to make a final volume of 1·2 ml. Uridine diphosphate glucuronic acid formation was determined by a procedure described previously (ref. 5). Results are expressed as μmoles formed per gm. of liver

Type of rat	No. of rats	*o*-Aminophenol glucuronide formed	Uridine diphosphate glucuronic acid formed
Jaundiced Wistar	6	0·008	4·9
Non-jaundiced Wistar*	8	0·034	4·3
Sprague–Dawley	7	0·061	5·8

* Non-jaundiced rats were litter-mates of the jaundiced animals.

Glucuronide formation was also examined in human subjects with congenital, non-obstructive, non-hæmolytic jaundice (ref. 1,*b*,*c*). Like the jaundiced rats described above, these subjects had a high concentration of free bilirubin in the blood, but no bilirubin glucuronide could be detected in the serum or bile. Glucuronide formation was studied by administering a substance that forms a glucuronide (N-acetyl *p*-aminophenol). Fig. 1 shows that the rate and magnitude of glucuronide formation in this syndrome is much less than in normal subjects. In addition, the rate of disappearance of the free compound from the plasma is delayed. Similar findings were obtained using tetrahydrocortisone as the aglycone[7].

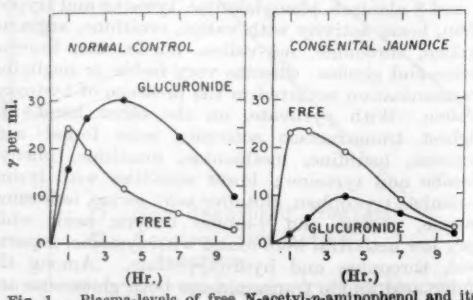

Fig. 1. Plasma-levels of free N-acetyl-*p*-aminophenol and its glucuronide. Each subject received 30 mgm. per kgm. of N-acetyl-*p*-aminophenol in a single oral dose. Free N-acetyl-*p*-aminophenol was determined by a procedure described previously (ref. 6). The glucuronide was hydrolysed by incubation with bacterial β-glucuronidase and the liberated compound determined

The observations described indicate that congenital non-obstructive, non-hæmolytic jaundice is a result of a reduced rate of glucuronide formation. Since bilirubin must compete with other normally occurring aglycones for a deficient glucuronide-forming enzyme system, the consequence of this defect is an accumulation of free bilirubin in the plasma.

A detailed report of this work will be given elsewhere.

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Utilization of 4-Amino 5-Imidazole Carboxamide in Plant Tissues

THE diazotizable amine which accumulated in cultures of *Escherichia coli* during sulphonamide bacteriostasis has been isolated and its identity with 4-amino 5-imidazole carboxamide has been established[1,2]. Evidence to show that this compound was not merely a product of aberrant metabolism but a normal precursor of purines has been obtained[3] and its role in purine biosynthesis is well established[4]. Recently, it was demonstrated that the carboxamide was rapidly utilized in rat liver homogenates and preparations from actively growing tissues[5,6]. The present report deals with the preliminary experiments carried out to assess the role of this compound as a potential precursor of purines in plants. Resting, as well as germinating, seeds of *Phaseolus radiatus* (green gram) were used in this investigation.

The plant tissues were homogenized thoroughly with 2–3 volumes of $M/15$ phosphate buffer, *p*H 7·4, centrifuged briefly at low speed and 1 ml. of the supernatant was incubated with an equal volume of a solution containing succinate ($2 \times 10^{-2}\,M$), formate ($2 \times 10^{-2}\,M$), niacinamide ($2 \times 10^{-2}\,M$), diphosphopyridine nucleotide ($4 \times 10^{-4}\,M$), adenosine triphosphate ($1 \times 10^{-2}\,M$), magnesium sulphate ($3{\cdot}0 \times 10^{-4}\,M$) and carboxamide ($2 \times 10^{-2}\,M$) for 4 hr. at 37° C. The reaction was arrested by the addition of 0·1 volume of perchloric acid (60 per cent). Residual carboxamide was estimated in the supernatants by the Bratton–Marshall reaction[7]. Sodium 1 : 2 naphthoquinone 4-sulphonate (Folin's reagent) as a reagent for carboxamide after paper chromatography[8] was also used. Protein estimation was done by the biuret method. The results are summarized in Table 1.

Table 1. UTILIZATION OF 4-AMINO 5-IMIDAZOLE CARBOXAMIDE BY EXTRACTS OF *Phaseolus radiatus*

Tissue	Resting seeds	Germinating seeds		
		24 hr.	48 hr.	72 hr.
Carboxamide utilized* μgm./mgm. protein/4 hr. at 37° C.	0·78	1·03	1·49	2·00

* Average of triplicate values

Thus preparations from germinating seeds were found to metabolize carboxamide to greater extents than resting seeds. This increased metabolism of carboxamide in germinating plants is of interest since tissue growth implies cellular multiplication which, in turn, according to all available evidence, involves the presence of nucleic acids. Investigations on the nature of the individual steps in the overall utilization of this compound in plants should be of interest. Further work on these aspects is in progress.

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Induction of Immunological Tolerance in Rats to Foreign Erythrocytes

THE term 'acquired immunological tolerance' was used by Medawar and co-workers[1] for describing the toleration of skin homografts in mice which had been injected *in utero* with a cell suspension from mice of the donor strain. Since then, many workers have tried to produce a similar tolerance to antigens which give rise to antibodies of the classical circulating type. Both positive[2–4] and negative[5–7] attempts have been reported. One of the systems that has been investigated recently is the anti-sheep erythrocyte system. Bauer *et al.*[7] have reported failure to produce immunological tolerance in rats by intra-uterine injection of fœtuses with sheep red cells. They point out that in many of the successful experiments quoted above, large doses of antigens had to be injected for prolonged periods to produce non-reactivity. They maintain that the whole range of phenomena included under the heading of immunological tolerance may well be an expression of the phenomenon of immune paralysis, such as can be produced by the injection of pneumococcal polysaccharides into mice[8].

We have been studying the effects of injecting neonatal rats with both mouse and sheep erythrocytes, starting the injections within 36 hr. of birth, and giving repeated doses twice a week for three to eight weeks. Using large doses (0·25 ml. of washed 20 per cent cells per injection, given intraperitoneally) we

Table 1. Rat Anti-Sheep Erythrocyte Titres

Prelim. bleed	After 1st course 1 week	After 1st course 2 weeks	After 2nd course 9 days	After 2nd course 3 weeks	After 3rd course 5 days	After 3rd course 9 days	After 4th course 1 week
93	<4	<4	50*	<4	<4	<4	<4
94	<4	<4	30*	<4	<4	16	<4
95	<4	<4	<4	<4	64*	48	20
96	<4	<4	20	<4	32	50	20
Cont. 1	<4	200	300	800	380	600	1,100	400
Cont. 2	<4	200	300	100	128	400	1,100	256
Cont. 3	<4	50	40	90	28	200	1,000	200

* Incomplete agglutination patterns only were obtained to this titre

were able to induce immunological non-reactivity quite uniformly in the animals treated for eight weeks, and somewhat less uniformly in the animals treated for three weeks. Table 1 gives the result of a typical experiment, using sheep erythrocytes. The treated animals were given two injections per week for eight weeks, and one week after the end of this course three intraperitoneal injections were given of 1 ml. of 20 per cent erythrocytes over a period of one week, using three normal animals of the same age as controls. The animals were bled from the tail one and two weeks after the last injection, and then given a further two injections, and bled nine days and three weeks after the latter injection. Six weeks later, the rats were again given an injection of 1 ml. of 20 per cent cells, and bled after five and nine days. Finally, at the age of five months, the rats were given a further injection of 20 per cent cells, and bled one week later. The antibody titres were expressed as the reciprocal of the dilution of serum producing partial agglutination of 1 per cent red cells at room temperature.

From Table 1 it can be seen that the treated animals produce very little antibody, even after four injection courses. If the neonatal injection course ceased after three weeks, somewhat different results were obtained. The majority of the animals were completely tolerant to one injection, at eight weeks, but after a secondary injection about half developed high antibody titres. Similar results were obtained using mouse erythrocytes. Rats given an eight-week neonatal course exhibited complete tolerance to primary, secondary, tertiary and quaternary stimuli. Those given a three-week course uniformly failed to produce antibody to a primary stimulus at eight weeks, but about half the animals produced fair titres after a secondary stimulus.

In order to exclude the possibility that the failure to detect circulating antibody was due to its removal by antigen leaking from tissue deposits, the rate of disappearance of passively transferred antibody was examined. Two litters of tolerant rats were inoculated with 0·5 ml. of hyperimmune serum, and the fall in titre examined in serum samples taken at two-day intervals. The rate of fall was identical in tolerant animals and normal controls. An attempt to produce true immune paralysis by injecting more mature rats with very large doses of sheep red cells was unsuccessful. It thus appears that the production of non-reactivity depends on starting the injections while the animal is immunologically immature, and continuing them well beyond the critical period.

Further work in this field is in progress, and will be reported in full in a later publication. I wish to express my thanks to Sir Macfarlane Burnet for his interest in this work. It was carried out under a grant from the National Health and Medical Research Council of Australia.

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Antimitotic Activity of 5-Tertiary Butyl Benzimidazolone

In chronic toxicity tests of several derivatives of benzimidazolone, the 5-substituted compounds were well tolerated, with the exception of the 5-tertiary butyl benzimidazolone. This substance caused retardation of growth in rats receiving the standard dose of 500 mgm./kgm./day by stomach tube, with death after 20–25 days of treatment. Hæmatological examination after the onset of the loss in weight revealed a severe anæmia and leukopænia, found at autopsy to be the results of aplasia of the bone marrow. Lymphoid atrophy was also seen; but other tissues showed no change, except for the presence in various organs of large numbers of mitotic figures.

A single oral dose of 5-tertiary butyl benzimidazolone 400 mgm./kgm. caused an increase in the percentage of mitotic figures in the bone marrow, which reached a maximum value of 6–17 per cent within 3–8 hr. and returned to normal by 14 hr. The marrow of untreated control rats showed only 1–2 per cent mitotic figures. This increased proportion of mitotic figures after 5-tertiary butyl benzimidazolone undoubtedly represents an actual arrest of mitosis. It resembles that produced by colchicine 1·5 mgm./kgm., except that fragmentation of the nucleus was evident in some 16 per cent of the cells 8 hr. after colchicine, but not after the former.

The antimitotic action of 5-tertiary benzyl benzimidazolone was almost unique in a series of some thirty related compounds tested by oral administration of a single dose of 400 mgm./kgm. Only 5-tertiary butyl benzimidazole showed a similar effect, but to a smaller degree. A sample of 5-tertiary butyl benzoxazolone did not affect mitosis, nor did the 1,3-dimethyl-substituted 5-tertiary benzyl benzimidazolone. Other compounds that gave a negative result in the test included the 5-methyl, 5-ethyl, 5-*n*-propyl, 5-*iso*propyl, 5-*n*-butyl, 5-*iso*butyl, 5-sec. butyl, 5-n. amyl, 5-*iso*amyl, 5-sec. amyl, 5-t. amyl, 5-phenyl, 5-chloro, 5-bromo, 5-amino and several di-, tri- and tetra-substituted benzimidazolones, as well as the unsubstituted benzimidazolone and benzimidazole.

5-Tertiary benzyl benzimidazolone was also tested for anti-tumour activity against the Gardner lymphosarcoma (*6C3H-ED*). Tumours of 1·8–3·2 c.c. (estimated) grew out in all the twelve control mice during ten days of the experiment, while twelve mice receiving 5-tertiary benzyl benzimidazolone, 400 mgm./kgm./day starting immediately after inocula-

tion, did not develop palpable tumours. Of the twelve controls with established tumours, half were then treated with 5-tertiary benzyl benzimidazolone in the same dose. Partial regression occurred after seven days of treatment. These studies are being continued.

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Chemical Nature of Parathyroid Hormone

Most of the data accumulated in the past thirty-two years[1] has led to the conclusion that parathyroid hormone is a protein. In 1954, Handler, Cohn and Dratz[2] attempted to purify this hormone by means of ion-exchange chromatography, but found hormonal activity associated with a number of protein peaks. On the basis of their results, they suggested that the hormonal activity might reside in a smaller molecule, presumably not necessarily nitrogenous, which readily absorbs on proteins. Raoul, Mornay and Prelot[3] have recently claimed to have prepared, by two different lipid extraction methods, a highly active material which did not contain nitrogen. On the basis of unreported evidence, they suggested that this active substance was steroidal in nature. Since the D vitamins, which are steroid, closely mimic, in some respects, the action of parathyroid hormone on bone and kidney, the possibility that this hormone is a steroid merits consideration.

Upon undertaking the problem of the isolation of parathyroid hormone, it seemed imperative to us to perform experiments to confirm, if possible, the work of Raoul *et al.*[3]. They claimed that it was possible to obtain non-nitrogenous extracts containing a specific activity of 300 u./mgm. by three means: (1) extracting an acetone powder, prepared by the method of L'Heureux, Tepperman and Wilhelmi[4], with boiling absolute ethanol for at least 30 min.; (2) extracting the same active powder with a mixture of ethanol and ether (3 : 1) at − 40° C.; and (3) extracting a hydrochloric acid extract of 'defatted' glands with ethanol–ether (3 : 1) at − 40° C. They further claimed that the nitrogenous residue in each instance was inactive. We have followed their extraction procedures as closely as possible, using methods (1) and (3). In each instance, the lipid extract was concentrated to a few millilitres by vacuum distillation, and then assayed, as were the nitrogenous residues. All fractions were assayed by the method of Davies, Gordon and Mussett[4], which depends on the rise in concentration of plasma calcium in parathyroidectomized rats 18 hr. after the test injection. No hormonal activity was found in any of the lipid extracts and approximately 80 per cent of the estimated original activity was found in the nitrogenous residues. The results are completely contradictory to those of Raoul *et al.*[3].

The important difference in these two sets of experiments is in the assay method employed. Raoul *et al.*[3] utilized the method of Dyer[6], in which normal rabbits are the test animal. Dyer's own conclusions about this method were that rabbits were unsuitable assay animals because of the marked fluctuations in the normal concentration of serum calcium, and the wide variation in response to a test injection of parathormone. This has been the experience of others[1].

Our findings in conjunction with further work in progress lead us to believe that the hormone is a small protein, probably in the size-range of adrenocorticotrophic hormone and insulin. Our more important reasons for this conclusion arise from our unpublished observations that a partially purified, highly active (100 u./mgm.) hormonal preparation contained 14 per cent nitrogen (micro-Kjeldahl) and 97 per cent of its weight was accounted for by its amino-acid content.

This investigation was supported in part by a grant (*A*1331) from the U.S. Public Health Service, and was carried out while one of us (H. R.) was a Research Fellow of the U.S. Public Health Service.

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Toxicity of Erythromycin

In the course of studies on antibiotic therapy of rickettsial infection in the guinea pig, it was found that oxytetracycline, chlortetracycline and tetracycline administered intramuscularly were tolerated well in the dosages employed. The administration of erythromycin on an equivalent dose-weight basis, however, resulted in death of a portion of the test animals. The picture observed was comparable to that noted by Kaipainen and Faine[1] following oral, intraperitoneal or intravenous administration of the drug. Because the response of the guinea pig to erythromycin appears to differ from a simple toxicity phenomenon, the following observations are reported.

Hartley strain albino guinea pigs weighing 300–400 gm. were employed throughout this work. These animals were obtained from a single source and were free of intercurrent infection with bacterial pathogens. They were maintained in a constant-temperature environment on rabbit chow (without antibiotic supplement—Ralston Purina Co.) and fresh greens. Erythromycin lactobionate (Abbott Laboratories—Lot No. 650–8938), reconstituted daily in water for injection (USP), was used. Injections were made into the hamstring muscles.

Initially, the drug in a dose of 1·5 mgm. twice daily for 9 days (total dose 27·0 mgm.) was started simultaneously with an intraperitoneal rickettsial challenge. Nine of the ten animals on erythromycin died between the eighth and eleventh day post challenge, several days prior to death of the control animals receiving only the rickettsial challenge.

A second series of guinea pigs were then given drug alone twice daily for five days. The dosages admin

Table 1. Effect of Initial Administration of Erythromycin to Hartley Strain Guinea Pigs for a Five-day Period

Total dosage (mgm.)	Deaths/total	Day of death*	
		Average	Range
7·5	8/15	8·6	8–11
15·0	6/15	9·3	9–10
22·5	8/15	9·6	8–11

* From administration of first dose.

istered and the results obtained are shown in Table 1. The day of death is measured from the time the first dose of drug was given. It is apparent that, in this dose-range, lethality and size of dose are not correlated.

Surviving animals showed no signs of illness. The affected animals, for several days prior to death, refused food, showed ruffled fur, and exhibited a diarrhoea. At autopsy the spleens of these animals were pale and markedly smaller than those of normal animals of the same weight. There were no other gross autopsy findings of note. In additional animals, similar signs and death have been observed to follow administration of as little as 1·5 mgm. of erythromycin.

The surviving animals from the drug regimen shown in Table 1 were observed for 2 weeks after cessation of the drug and appeared normal in all respects. At this time an identical schedule of drug administration for 5 days was re-instituted. This second administration of erythromycin did not produce illness and all animals survived.

The cause of the 'all-or-none' response of these guinea pigs to erythromycin is not apparent. Since other work does not permit further studies at this time, the findings are reported as a matter of record.

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Identical Nature of the Leucocyte Antigens detectable in Monozygotic Twins by means of Immune Iso-Leuco-agglutinins

The presence of anti-leucocyte antibodies, which are capable of causing *in vitro* the agglutination of certain varieties of leucocytes, and which are inactive on the patient's own leucocytes[1,2], is often observed in the blood of polytransfused patients.

Using 28 human sera containing immune iso-leuco-agglutinins of this type, we studied the leucocyte antigens of four pairs of twins. (We are grateful to Prof. M. Lamy for allowing us to study the blood of these twins.)

Table 1 shows the identical reactions obtained in each pair of monozygotic twins. Comparison with the reactions obtained with a pair of dizygotic twins revealed marked differences.

Confusion caused by the presence of anti-red cell antibodies in the leuco-agglutinating sera were overcome. The naturally occurring antibodies, anti-A, anti-B, or anti-$A+B$, were absorbed or neutralized beforehand by the water-soluble substances A and B. In the same way, four of the sera used in this study contained irregular antibodies active on red cells (anti-D, anti-C). Numerous other sera containing similar antibodies but without leuco-agglutinins were tested against the leucocytes of donors having the corresponding red-cell antigens always without producing leuco-agglutination. These results suggest the hereditary transmission of the leucocyte characteristics, probably determined by special genes. A study of this mode of transmission in several generations is in progress.

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Table 1. Agglutination of the Leucocytes of Twins with the Aid of Leuco-agglutinating Sera

		Monozygotic twins: Leuco-agglutinating sera																										
		Au	*Ch*	*Ce*	*Le*	*Di*	*Ma*	*So*	*Le*	*Dr*	*Pa*	*Du*	*Lm*	*Bo*	*Te*	*Ro*	*De*	*Bn*	*Mg*	*Me*	*Bu*	*Ds*	*Rb*	*Be*	*Vc*	*Ba*	*Ca*	*Ve*	*Pu*	*Lx*
P.	Va	−	±	−	+	−	+	+		−		+		+	+	+	−	+	+	+	±			+		+	+	+	+	+
J.	Va	−	±	−	+	−	+	+		−		+		+	+	+	−	+	+	+	±			+		+	+	+	+	+
		Red cell groups: AB Cc D ee Fy(a−) K− M P																												
E.	Ro	+	±		−	−		+	+	±	−	+	+	+		+	−			+	+	+	+	+		+	+	+		
H.	Ro	+	±		−	−		+	+	±	−	+	+	+		+	−			+	+	+	+	+		+	+	+		
		Red cell groups: A cc dd ee Fy(a−) K− M N P																												
D.	Te	+	+		(+)	+		+	+	−	+	+	+	+		−	−			+	+					+	+	+		
B.	Te	+	+		(+)	+		+	+	−	+	+	+	+		−	−			+	+					+	+	+		
		Red cell groups: A CC D e e Fy(a−) K− N P																												
		Dizygotic twins																												
L.	Go	+	+		−	+		+	+	+	−	+	+	+	−	−	−		+	+			--	−	+	+	+	−		+
V.	Go	+	−		+	+		−	+	+	−	−	+	+	+	+	+		+	+			+	+	+	+	+	+		+
		Red cell groups: L. GO: A Cc D ee Fy(a−) K− N P V. GO: A cc D Ee Fy(a−) K− N P																												

Ultra-violet Irradiation of Dry Tobacco Mosaic Virus

We have previously reported that the infectious nucleic acids obtained from different strains of tobacco mosaic virus have the same sensitivity to inactivation with ultra-violet light[1]. The intact strains, however, differ in this regard[2]. Strain *U*2 has the same sensitivity as the infectious nucleic acid, whereas strain *U*1 is 5½ times more resistant. It was therefore concluded that the type of combination between protein and nucleic acid that exists in the *U*1 strain affords appreciable protection from the damaging effects of ultra-violet light.

Since several reports have appeared in the literature which indicate that certain organisms are more sensitive to inactivation with ultra-violet light when irradiated dry than when irradiated wet[3–5], a study was undertaken to determine whether the protection against ultra-violet light damage, observed for the *U*1 strain, is related to the presence of water during the irradiation.

The technique for the wet irradiation of the tobacco mosaic virus strains has been described[2]. The following technique devised for dry irradiation gave the most consistent results. A 0·05 per cent virus suspension was prepared in *M*/15 phosphate buffer, *p*H 6·9–7·0, containing 0·01 per cent crystal-

line bovine serum albumin as a pipetting aid. Aliquots of 0·01 ml. were pipetted on to 18 mm. circular cover-glasses. The droplets were allowed to dry in the laboratory until liquid was no longer visible. Each cover-glass was then placed into a small individual drying chamber which was constructed by glueing a 24-mm. diameter, 10-mm. high glass cylinder to a microscope slide with Armstrong's adhesive *A*–6. A smaller cylinder, 15 mm. diameter, 5 mm. high, placed within the larger cylinder, served both as a well to contain phosphorus pentoxide and as a support for the cover-glass. The chamber was closed by sealing a 2-mm. thick quartz square to the top of the larger cylinder with vacuum grease. 2–3 hr. after the chambers were sealed, the dry virus was irradiated by placing the chambers 24·5 cm. from a Westinghouse germicidal lamp, 782*L*–30, the output of which is primarily at 2537 A. After irradiation, the cover-glasses were placed in 5 ml. of *M*/15 phosphate buffer, *p*H 6·9. Approximately 3 hr. was allowed, with occasional stirring, for resuspension of the virus, before assaying it for infectivity.

In different experiments 30–100 per cent of the virus infectivity was recovered after the drying and resuspension procedure. The presence of albumin was found not to interfere with the results of the irradiation experiments.

As shown in Fig. 1, the sensitivity of the *U*2 strain to inactivation with ultra-violet light is the same whether irradiated wet or dry. However, the *U*1 strain increases in sensitivity 5½ times when irradiated dry. Thus, both strains have identical sensitivities when irradiated dry.

The change in the sensitivity of the *U*1 strain upon drying is reversible. After first drying and then rewetting before irradiation, the *U*1 strain recovers its initial wet sensitivity. These results also appear in Fig. 1.

The results of these experiments demonstrate that the type of protection against ultra-violet light damage that exists in the *U*1 nucleic acid–protein combination is operative only when the virus is wet and is lost upon drying.

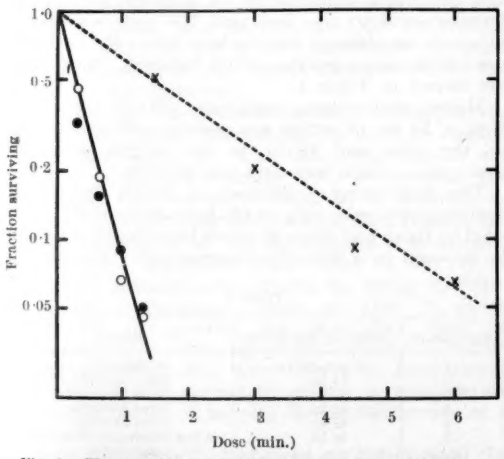

Fig. 1. The sensitivity to inactivation by ultra-violet light of tobacco mosaic virus strains *U*1 and *U*2 irradiated wet and dry. The solid and broken lines represent previously published data (ref. 2) for the wet sensitivity of strains *U*2 and *U*1, respectively. ○, *U*1, dry; ●, *U*2, dry; ×, *U*1 dried and rewetted before irradiation

A possible explanation for the difference in sensitivity of the two intact strains is that the *U*1 strain may exist in a more hydrated state than the *U*2 strain. Consequently, the *U*1 strain may be less dense than the *U*2 strain. We have explored this possibility by equilibrium centrifugation of a mixture of the two strains in a density gradient as described by Meselson *et al.*[6]. Contrary to the hypothesis, the results of this experiment demonstrate that the *U*1 strain is actually more dense than the *U*2 strain.

Hollaender and Dugger[7] report an ultra-violet action spectrum for tobacco mosaic virus which departs markedly from the absorption spectrum of nucleic acid. This is in contrast to the results obtained with several other viruses and micro-organisms[8]. However, the common strain (*U*1) was irradiated in solution for the determination of the action spectrum, a condition which is shown here to protect the virus from ultra-violet damage. It is possible that the action spectrum for the *U*2 strain or for the *U*1 strain irradiated dry may conform more closely to the absorption spectrum of nucleic acid.

Kaplan and Kaplan[5] suggest that the increased efficiency of ultra-violet light in killing dry *Serratia marcescens* may be due to a change in the structure of the deoxyribonucleic acid of these cells. The current experiments raise the possibility that in *Serratia* and other organisms the protein to which the nucleic acid may be attached plays a part in determining the sensitivity of the nucleic acid to the damaging effects of ultra-violet light.

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Subendothelial Space between the Ovarian Interstitial Cell and the Endothelial Lining of the Blood Sinusoids

RECENT electron microscopic investigations have demonstrated the peculiar relation between endocrine cells and capillary blood vessels. The cell plasma membrane of the former is not directly in contact with the endothelium of the latter: there is a perivascular space between both. These peri-capillary spaces were first described by Lever[1] in ultra-thin sections of the adrenal cortex and medulla. The same subendothelial space is also found in the thyroid and parathyroid[2] and in the corpus luteum[3]. It was observed by Green and van Breemen[4] in the adeno-hypophysis.

During an experimental study on the endocrine function of the interstitial cells of the rat's ovary, we tried to find out whether this subendothelial

space was demonstrable between those cells and the endothelial lining of the capillary vessels.

Young, normal albino rats were used. The tissues were fixed in an osmic solution according to Palade, dehydrated in alcohol, embedded in methacrylate and sliced with a Sjöstrand ultra-microtome. A Philips 100 *EM* electron microscope was used for the microscopy.

At several places an irregular space is seen between an interstitial cell and the capillary endothelium. This space is about 3500 A. wide. It is rather remarkable that the cell, on the side turned towards this space, is provided with many irregular protoplasmic threads, which are in contact with a great number of microvilli, developed on the endothelium of the capillary vessels. The mazes between those microvilli are rather lightly coloured, while there are here and there dark-stained granulations, showing no tendency to form a regular row.

We believe we have added to the already existing evidence concerning the internal secretion of the interstitial cells of the ovary, namely, the existence of a perivascular space similar to that described by the above-mentioned authors in preparations of endocrine tissues.

A detailed description of this perivascular space and of the variations of its size according to the experimental environment will be published later.

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Effect of Desiccation on the Eggs of *Simulium damnosum*, Theobald

In the northern territories of Ghana and other savannah areas of West Africa, many of the smaller rivers which form the breeding places of *Simulium damnosum* in the rainy season are liable either to dry up completely in the course of the long dry season or to be reduced to a series of stagnant pools unsuitable for breeding. When these streams start to flow again at the onset of rains, the rapid appearance of *Simulium* larvæ, sometimes within a week of flooding, has long posed the question of the exact stage or condition in which *Simulium damnosum* survives the long dry season in those areas. The whole question, along with all the relevant literature, has been discussed fully by Crisp[1].

For a long time the most popular explanation was that the season of drought was passed in the egg stage, the eggs lying dormant in the dried mud or sand of the water-course. In order to test this point, Edwards[2] collected samples of sand and silt from the beds of rivers which five months earlier had formed breeding places of *Simulium* larvæ, but which had been dry for three months at the time of collection. Fifty-four samples were pooled and immersed in water in a larva-rearing tank; three days later three *Simulium* larvæ were seen, and later an imperfect adult emerged which could not be identified.

Lack of information about the egg-laying sites and egg-laying habits of *Simulium damnosum* in West Africa has long held up any direct approach to this question by means of controlled experiments on the eggs themselves. In addition, *Simulium damnosum* is very refractory in captivity. It is only rarely that gravid females will lay eggs in confinement, and the eggs, if they do hatch, do not appear to develop normally. No real progress was made in this direction until Crisp[1] carried out a detailed study of *Simulium damnosum* in Ghana. Crisp dried out batches of *Simulium damnosum* eggs from natural ovipositing sites, and with material from thirty ovipositions found that eggs could survive up to 40 min. exposure to direct sun, but that with longer exposures an increasing proportion of the eggs failed to hatch. Eggs allowed to dry and remain in the sun for 12 hr. never hatched. This finding, together with the fact that he was never able to recover any eggs from 100 samples of sand taken from breeding sites at the beginning of the dry season, led him to conclude that "the possibility of dry season survival in the egg stage seems unlikely".

In Liberia, I was able to study the ovipositing habits of *Simulium damnosum*[3] and to obtain from time to time very large batches of *Simulium damnosum* eggs from natural breeding sites. These observations were made in rubber plantations in the rain forest area where *Simulium damnosum* breeds through the entire year in streams and small rivers which never dry up.

A series of simple experiments was carried out to study the reactions of these eggs to the effects of desiccation. Leaves, with egg batches containing many thousands of eggs, were divided into portions and allowed to dry in beakers in a shaded part of the laboratory at a temperature of 27°–28° C. and approximately 70–95 per cent relative humidity. After different periods of drying, the portions of leaf were suspended in contact with water agitated by a stream of air bubbles. Under these conditions untreated controls always showed a complete hatch. In those cases where the time of oviposition was known the eggs used were 16–24 hr. old. (The egg stage may take as long as 65 hr. in Liberia.) Owing to the very large number of eggs in these batches—the combined ovipositions of a large number of females—and to the fact that the eggs were piled in layers, no attempt was made to count the numbers used or the exact number which hatched. The results are shown in Table 1.

Hence, under these conditions, periods of desiccation of 24 hr. or longer are usually sufficient to kill all the eggs, and 48 hr. is the longest period of desiccation which any eggs can survive.

The desiccating conditions to which these eggs were exposed were very much less severe than those used by Crisp and those to which they would normally be exposed in a dried-up water-course. The results

Table 1

Experiment	Period of desiccation	Result
1	Up to 18 hr.	All hatched
2	24 hr.	None hatched
3	24 hr.	None hatched
4	42 hr.	None hatched
5	48 hr.	None hatched
6	48 hr.	A few hatched from a very large batch
7	3½ days	None hatched
8	4 days	None hatched
9	6 days	None hatched
10	6 days	None hatched

endorse those of Crisp and indicate that the eggs of *Simulium damnosum* show no marked ability to withstand even comparatively short periods of exposure to desiccation.

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Gonad Temperature and Spontaneous Mutation-rate in Man

SINCE the spontaneous mutation-rate is known to vary with temperature, the present investigation was conducted in order to clarify the degree to which the temperature of human genetic material might vary under different environmental conditions.

For an average sex-linked lethal mutation in *Drosophila melanogaster*, Timoféeff-Ressovsky and Zimmer[1] report a Q_{10} of 6·5. This value is largely in agreement with Muller's[2] earlier data, though somewhat higher. Although the question as to the influence of temperature on the spontaneous mutation-rate is not yet fully elucidated (cf. discussions by Stubbe[3] and Wittmann[4]), the most important negative results seem to concern particular cases, for example, labile genes[5]. Radiation-induced mutations are virtually independent of temperature, except under extreme conditions. The X-ray dose which doubles the mutation-rate amounts, in the species hitherto studied (for example, *Drosophila melanogaster*, mouse, and barley), to about 100 r., whereas the average background radiation amounts to not more than 0·1 r. per year[6]. If 30 r. is taken as a low value for the doubling dose in man[6], ionizing radiations will be responsible for not more than about 10 per cent of the spontaneous mutation-rate. The remaining 90 per cent will presumably exhibit dependence upon temperature similar to that demonstrated for *Drosophila*. Even a comparatively small temperature variation in the genetic material would therefore affect the mutation-rate appreciably.

In mammals the testes are usually, at least during the mating period, situated in the scrotum outside the peritoneal cavity. The temperature inside the scrotum is regulated at 2–5° C. lower than the peritoneal temperature[7]. That it is possible to influence the testicular temperature from outside has been demonstrated by the experiments of Moore and co-workers[8]: treatment with water at 47° C. or insulating material was shown to cause sterility. From an evolutionary point of view it seems reasonable to consider the possibility that, in addition to the unique metabolic stability of deoxyribonucleic acid[9], the lower testicular temperature and the sterility caused by a rise in temperature constitute means of keeping the mutation-rate at a low level.

In an exploratory experiment we investigated the effect of normal clothing on the scrotal temperature of men aged 20–40 years. The measurements were made partly with a thermocouple, partly with a 1,000 Ω N.T.C. resistor, the instruments being taped to the skin of the distal part of the scrotum. A skin fold was then produced, allowing the temperature to be measured between the testes. In order to exclude the possibility of the temperature regulation being dependent on adaptation, one series of measurements was done (outdoors) on nudists who had lived for more than two weeks in a nudist camp, unclothed except during bad weather. Since no difference in temperature regulation was found between the nudists and non-nudists who were studied concurrently, a second (indoor) experiment was performed with non-nudists alone. After disrobing or clothing, the temperature was found to reach a constant value within 1–2 hr. (Fig. 1). In both series the environmental temperature ranged between 19·5 and 21·5° C.

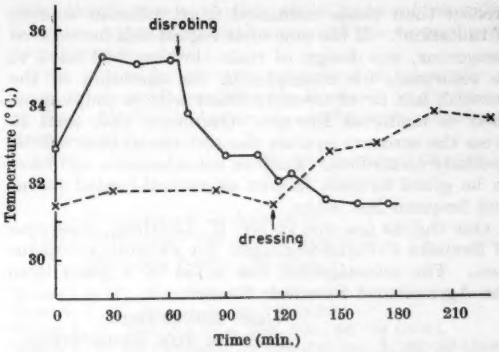

Fig. 1. Typical individual curves showing the change of scrotal temperature due to dressing and disrobing. Full line, non-nudist; dotted line, nudist

The results are shown in Table 1. The values certainly represent the testicle temperature, since they compare well with data obtained in measurements on different animals[7,8]. Results from the two series were lumped and a highly significant difference was found, amounting to 3·3±0·4° C. between the clothed and disrobed states.

The observed difference in temperature gives at least the order of magnitude of the rise in temperature affecting the genetic material of that part of the human race which wears clothes of European type. If we assume a Q_{10} of 6·5 to be valid for the spontaneous mutation-rate of an average gene, the observed difference would correspond to an increase of about 85 per cent in the mutation-rate, in so far as mutations are transmitted by the male. The fact that our modes of dress have been predominant for several centuries might explain almost half the present load of spontaneous mutations. We thus see how modes of dress based chiefly on sexual taboos might imply genetical hazards 100–1,000 times

Table 1. SCROTAL TEMPERATURE OF CLOTHED AND UNCLOTHED SUBJECTS

Experimental conditions	No. of subjects	Mean scrotal temperature (°C.)		Difference between clothed and nude (° C.)
		Clothed	Nude	
Outdoor experiment:				
Trained nudists	5	33·9	30·7	3·2
Parallel controls	3	34·3	30·9	3·4
Indoor experiments:				
Controls only	7	34·0	30·5	3·4
Total	15	34·0	30·7	3·3
Standard error		±0·15	±0·45	±0·39

greater than those estimated from different sources of radiation[9]. If the eugenists regard this increase as dangerous, the design of male clothing will have to be reformed, for example, in the direction of the Scottish kilt or of trousers fitted with a codpiece as used in medieval Europe. Garments that tend to press the scrotum against the abdominal skin will be specially hazardous. Further consideration will have to be given to such factors as central-heated rooms and frequent hot baths.

Our thanks are due to Mr. K. Lindberg, chairman of Svenska Friluftsföreningen, for valuable co-operation. The investigation was aided by a grant from the Agricultural Research Council.

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Resumption of Gonadotrophic Function in Pituitary Grafts following Re-transplantation from Kidney to Median Eminence

It has been repeatedly demonstrated that the pars distalis of the hypophysis suffers great functional and cytological losses whenever it is transplanted to a site remote from normal. Thus, FSH and LH secretion ceases abruptly. Everett[1,2] has demonstrated in rats that luteotrophin is the only gonadotrophin secreted during 2–3 months after auto-transplantation to the kidney. As early as 8 days following transplantation, histological examination of the grafts indicated complete lack of basophils and the presence of only small 'acidophils' and chromophobes. One may question whether these functional and cytological changes result from operative trauma and other adverse effects of transplantation, on one hand, or from loss of hypothalamic control, on the other hand.

To study this question the following experiment was performed using 27 albino female rats, 13 experimental and 14 controls. In all animals hypophysectomy was performed on a given day, the posterior lobe was discarded and the pars distalis was transplanted to the kidney capsule. 15–25 days later the pituitary graft was removed from the kidney and by the trans-temporal approach it was re-transplanted under the brain. In experimental animals it was placed under the median eminence of the tuber cinereum and in controls under the temporal lobe. Up to this time, daily vaginal smears showed a constant anœstrus which continued in all animals even after re-transplantation. When no cyclic vaginal changes were observed for one month following this operation the assumption was made that the hypothalamus had reverted to a pre-pubertal state. Knowing that œstrogen injection accelerates onset of puberty it was decided to test the effect of œstrone on these animals. Very small doses (10–15 μgm. in sesame oil) were administered at irregular intervals of 5–18 days during a month and a half. The result was that in five experimental animals, cyclic œstrous changes began after 1–5 injections. These cycles were of 6–8 days duration. In addition to the cycles, further proof that gonadotrophic hormones were secreted in considerable amounts was given by the fact that three of these animals became pregnant. The remaining experimental animals and all the controls were injected with œstrone at intervals for periods of 2–3 months, but except for the days immediately following injection their vaginal smears always showed a complete anœstrus.

Histologically, the ovaries, uteri and vaginæ appeared normal in those animals that re-cycled following re-transplantation of the pituitary under the median eminence. On the other hand, these organs appeared completely atrophic in the control animals and also in those experimental animals that failed to show cyclic vaginal changes. In the cycling group, the appearance of the ovaries corresponded to the day of the cycle when the animal was killed. In general there were growing follicles and fresh corpora lutea together with some repair of the interstitial tissue. Fig. 1*a* shows a section of an ovary from a re-cycling animal killed in pro-œstrus in which numerous follicles and corpora lutea of different sizes can be seen. Fig. 1*b* represents an ovary from the control group where complete atrophy of the organ is evident.

To facilitate the study of vascularization of the re-transplanted grafts the animals were injected with india ink at the time of autopsy. Thick, unstained celloidin sections were examined, and it was seen that grafts from animals that had re-cycled derived their main blood supply from the primary capillary plexus of the median eminence. It was found that in only one of the remaining experimental animals the main

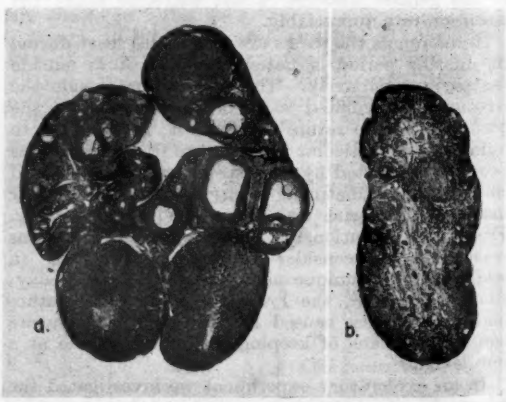

Fig. 1. (*a*) Ovary from a rat that re-cycled following re-transplantation of the pituitary graft under the median eminence. Pro-œstrus. Numerous follicles and corpora lutea of different sizes (× *c.* 16). (*b*) Ovary from a control animal following re-transplantation under the temporal lobe (× *c.* 16)

blood supply came from the median eminence region. The other grafts were so placed, for example too anteriorly, that only a very minor portion of the gland appeared to be irrigated by median eminence blood. Grafts from control animals received their blood supply from the overlying temporal lobe tissue. Although the source of blood was different the degree of vascularization of all grafts was in general equal. In size also there was little variation.

A great difference, however, between the grafts was seen on cytological examination of thin sections alternating with the thick ones described above. The grafts under the temporal lobe were composed of small, relatively undifferentiated cells, and the general appearance was very similar to the kidney grafts before re-transplantation. On the other hand, in the five grafts re-transplanted under the median eminence with restoration of cyclic function, great cellular re-differentiation was always found and basophils of normal form and staining properties were seen in significant numbers. Only one graft of the remaining experimental animals, one in most intimate relation to the median eminence, contained numerous large differentiated cells. All the others showed only occasional such cells, which were perhaps limited to the region vascularized by vessels from the median eminence. In all grafts from experimental animals failing to cycle, no normal basophils were found, the only ones present being castration cells.

Pituitary capsules were examined histologically and no remnants, or only very small ones, were found in three re-cycling rats and ten others. These consisted of small clusters of cells which were almost or completely undifferentiated. In the three re-cycling animals that had remnants these were in no case larger than the remnants found in other animals. On the contrary, in three of the control animals the remnants were at least three to four times larger than those from the experimental animals and they were well differentiated. Yet, even that amount of original gland left in place was incapable of appreciable gonadotrophic function as judged by the complete atrophy of the ovaries in these animals.

In an early experiment Greep[3] suggested a direct hypothalamic influence on gonadotrophin secretions. Normal reproductive function was sustained in hypophysectomized rats in which grafts were placed in the presumably emptied hypophysial capsules. Histological control of the extent of the hypophysectomy was impossible, however. This difficulty was circumvented by Harris and Jacobsohn[4], who introduced the transplant under the median eminence by the trans-temporal route, hence outside the hypophysial capsule. The capsule could then easily be searched for glandular remnants. The present experiment carries the work of Greep and of Harris and Jacobsohn one step further. It demonstrates that a pars distalis autograft, after having lost most of its functional and cytological differentiation while in the kidney, can recover nearly normal cytology and gonadotrophic function when re-transplanted from the kidney to the proximity of the median eminence.

One may conclude, therefore, that the loss of cytological differentiation and of FSH–LH secretion in pituitaries transplanted away from the hypothalamus is not primarily due to the injury which occurs during the operation, but rather to the distance from the diencephalon. This experiment furnishes strong additional evidence that to function normally the pars distalis must receive some humoral stimulus from the hypothalamus by way of the hypophysial portal vessels.

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Red-Cell Survival in Familial Hæmolytic Anæmias

When the red-cell hæm of familial hæmolytic anæmia patients is isotopically tagged, as by the administration of glycine-^{15}N, the curves of subsequent isotope-levels are interpretable in at least two ways[1]. It is shown here that the one of the interpretations which is most widely accepted is also consistent with the related data on tagging of the excreted stercobilin. This result combines with other data to imply that the incorporation of hæm occurs only during a relatively late part of the development of red cells in the bone marrow of these patients.

The case of sickle-cell anæmia studied by James and Abbott[2] is the easiest of such cases to interpret because the tagged hæm and stercobilin decay curves are the simplest ones yet available. But even for this case the tagged hæm curves appeared to have two possible interpretations[1]. If b is such that $1/b$ is the average time lapse between tagging and release of the developing red cells, and k is such that $1/k$ is the average survival time of circulating red cells, then the two alternative cases are such that either :

$$\text{I}\ \begin{cases} 1/b = 2 \text{ days} \\ 1/k = 19 \text{ days} \end{cases} \quad \text{or} \quad \text{II}\ \begin{cases} 1/b = 19 \text{ days} \\ 1/k = 2 \text{ days} \end{cases}$$

In an earlier note[1] I showed that if one assumes that the average development time of red cells is about the same as the average time lapse between their tagging and their release to the circulation, then the well-known bone marrow hyperplasia of familial hæmolytic anæmia cases is consistent with case II rather than case I. However, if we now consider the associated curve of tagged stercobilin we notice that k equals the fraction of tagged hæm converted to stercobilin (tagged) each day.

On further examination of the sickle-cell anæmia case described by James and Abbott[2], we find that approximately

$$0{\cdot}17 \times 0{\cdot}41 = 0{\cdot}07$$

is the fraction of hæm that was converted to stercobilin each day by that patient. Since $1/k = 14$ days in that instance, it must be concluded that the stercobilin data are consistent with case I above, which is also the generally accepted interpretation of such cases. Hyperplasia of the bone marrow is also consistent with this interpretation if the incorporation of hæm occurs only in the later stages of red cell development in the bone marrow.

A corollary of the conclusion that red cell survival in the circulation is 2–3 weeks in familial hæmolytic anæmia cases (and that incorporation of red cell hæm takes only the last few days of their formation) is that reticulocytes may circulate as long as 3–4 days, as in the case reported by James and Abbott[2].

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Effect of Exteroceptive Factors on the Œstrous Cycle of Mice

A study of the incidence of copulation plugs in monogamously paired mice showed that the œstrous cycle is influenced by stimuli associated with males[1]. These stimuli are probably olfactory since they are effective through a wire grid and removal of the olfactory bulbs results in a reduction of ovarian weight and activity[2].

It has now been established from changes in vaginal smears that the œstrous cycle is shortened by the proximity of a male, although a previous attempt to demonstrate this had failed[1]. The reason for this failure has also become apparent; for it has been found that when females are caged together in large groups, remote from males, œstrus and ovulation occur infrequently. Under such conditions the majority of animals show persistent mucification of the vaginal epithelium. In contrast to this, normal cycles occur regularly in most animals caged individually. This difference is also reflected in the incidence of mating when the mice are afterwards paired with vigorous males. In mice that have been grouped, copulation is synchronized so that in the majority it occurs on the third night after pairing, but is distributed more evenly over the first four nights in females which have been caged individually.

Mucification of the vagina of mice caged in groups and segregated from males may persist for forty or more days. There is an associated reduction in the weight of both uterus and ovaries. The latter appears to result from a decrease in the number of corpora lutea, which may be completely absent from some ovaries. These findings show that the œstrous cycle is suspended in these mice. The duration of the mucification, the ovarian and uterine changes, and in addition the failure of the uterus to respond to trauma with the formation of placentoma, show that this suspension is not due to pseudopregnancy. Thus it differs from the findings described by Lee and Boot[3] when mice were placed four to a cage. It seems probable that the mucification of the vagina resembles that observed by Robson and Wiesner[4] following the administration of doses of œstrogen too small to elicit cornification of the vaginal epithelium.

Stress from overcrowding does not appear to be the cause of the inhibition of the cycles for the following reasons: the animals maintain their weight and sleek appearance; there is no impairment of reproductive capacity since more than 90 per cent of them are capable of fertile mating within five days of pairing; if a male is confined in a grid within the cage œstrus appears promptly in almost all the mice.

These findings lead to the conclusion that the suspension of œstrous cycles of mice which have been grouped results from a relatively specific depression of pituitary gonadotrophic function. There is as yet no indication of the mechanism involved. However, if mutual inhibition of œstrous cycles also occurs in natural populations it may provide a mechanism, intrinsic to a species, to account for cycles in population density. While initiation of œstrous cycles by olfactory stimuli emanating from males may act as 'releasers'[5], Sibley[6] has pointed out that they may function also as 'isolating mechanisms'[7].

A full account of these findings will be submitted shortly to the *Journal of Endocrinology*.

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The Genus *Cypraea*

Recent literature abounds with criticism of the current trend to split genera. The subfamily Cypraeinae (family Cypraeidae) is a case in point[1,2]. Linnæus's genus *Cypraea*, which forms the basis for the subfamily, contained 42 species. At present approximately 160 are recognized. These species have been distributed in no fewer than 60 genera over the past twenty-five years, 52 of which appear in the latest work on the group[3].

While deploring the situation and suggesting that caution be used henceforth in describing genera, critics have failed to recognize two points. The genera among which the species of the Cypraeinae are now distributed are based primarily on only one feature of the animal, the shell, with little or no consideration of other characters such as the radula or genitalia. Secondly, numerous genera described on the basis of minute differences in shell characters which are necessarily of a somewhat subjective nature only serve to obscure the broad picture of prosobranch relationships.

Current studies of the soft parts of more than fifty species of the Cypraeinae show a remarkably conservative anatomical picture: the mantle is large and tends to cover the shell; the osphradium is trifid, enclosed in a single, arched ctenidium; the cerebral and pleural ganglia are closely associated; the pedal ganglia form long cords traversing the length of the foot; the penis is a slender, elongate, conical structure; and the digestive system is characterized by a swollen mid-œsophagus and stomach with a cæcum. The only differences discernible between species, apart from slight variations in mantle decoration, are in the structure of the radular teeth and in the pattern of the female genitalia. The species examined thus far fall into only two groups, one in which the female genitalia are

simple and the radular teeth rectangular with both subtending and internal bracts, and a second in which the female genitalia are complex in that a bursa copulatrix is present and the radular teeth are either rounded or rectangular and lack subtending bracts.

The conservative anatomical picture displayed is in marked contrast to the diversity implied by the numerous genera among which the species are now distributed. Furthermore, the two anatomical categories which are distinguishable cross the generic lines of the schemes of classification proposed by Thiele[4], Schilder and Schilder[5], Steadman and Cotton[6], and Allan[3]. These facts indicate that the numerous genera described primarily on the basis of shell characters are untenable.

I propose that only the genus *Cypraea* be retained for members of the subfamily Cypraeinae. This genus can be broadly described on the basis of both conchological and anatomical characters, and thus described becomes a useful and significant taxonomic category. It obviates burdening the literature with innumerable genera which cannot be definitively described on the basis of shell characters alone. Based on several features of the animal, it is significant when considered both in relation to other members of the family Cypraeidae and to the prosobranchs in general. Differences which do exist in radula and genitalia may be utilized in conjunction with certain conchological characters to describe subgenera at a later date.

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A Method for concentrating Pollen Grains and Small Fossil Remains from Fibrous Peats and Moss Polsters

ONE of the greatest factors retarding palynological studies of Australian Quaternary deposits is the difficulty in obtaining fossil pollen in concentrations sufficiently high for statistical analyses.

A modification of the standard sieving technique for peats[1] has been developed for extracting pollen and other small plant remains (for example, seeds, epidermal tissues and fungal fruiting bodies) from fibrous peats in Western Australia.

The method involves the use of small wire gauze tubes into which the peat is placed. The tubes are then boiled in 10 per cent alkali (potassium hydroxide) and as the peat digests, the pollen and other fine fragments pass through the meshes of the gauze, leaving the larger remains in the tube. The pollen fraction is then centrifuged and treated by the standard acetolysis and oxidation methods[1,2]. The plant remains retained in the tube are removed by inverting it in a small phial containing 20 per cent aqueous glycerine. A quick shake is sufficient to dislodge the residues, which can be stored for future examination. The gauze slug must be thoroughly cleaned before re-using and this is achieved with a bottle brush the bristles of which are trimmed to the same diameter as the gauze sieve tubes.

Three types of tube, made from brass gauze to withstand the alkali treatment, have been used and the method of construction is outlined below.

(*a*) *For peats. Tube A.* A small cylinder is made from a strip of 60-mesh gauze approximately 25 mm. × 27 mm., and the seam soldered (rolling the gauze around a pencil makes a tube of convenient diameter). A gauze disk is then soldered to one end of the tube and a small rubber stopper fitted to the other.

Tube B. A slightly larger tube is made in the same way as *A*, using a strip of 35 mm. × 40 mm. 100-mesh gauze.

(*b*) *For moss polsters. Tube C.* A large tube is made using a strip (approximately 65 mm. × 65 mm.) of 60-mesh gauze. This tube is particularly valuable where statistical comparisons of size are to be made between pollen grain and pollen preparations from anthers, where uniform treatments are essential.

The main advantage of sieving is that it allows the separation of the pollen from the larger organic fragments which break down during the later stages of treatment to residues which obscure and dilute the pollen. To test the value of the sieves described, three pollen preparations were made from the same peat specimen. The first, or control preparation, was treated by the standard alkali, acetolysis and oxidation methods. The second preparation was treated in the same manner as the control with the exception that the peat was placed inside tube *A* during the alkali treatment. In the third preparation, tube *A* was placed inside tube *B* for the alkali treatment. An estimate of the concentration of pollen in the preparations was made by counting the ratio of the frequency of pollen to non-pollen material encountered by a micrometer eyepiece mark in a series of ten transects across an 18-mm. square coverslip. By comparison with the control preparation, the 60-mesh cylinder gave a 600 per cent increase in pollen frequency while a 1,500 per cent increase was obtained by placing tube *A* inside tube *B*.

When the peat was boiled directly inside the tube *B* it tended to block the meshes, preventing the finer material from passing through. Thus the principle of the modified method is the same as in mechanical analyses, where the coarser fractions are removed before proceeding to successively finer fractions, and this process continued until the desired size is reached.

The advantages of the gauze tubes over the more conventional sieving techniques appear to be two-fold. First, the filtering process combines boiling in alkali and filtering into a single operation. Thus only the volume necessary for the alkali treatment is required and the time-consuming washing of residues and reconcentration from the filtrate eliminated. Secondly, continuous agitation prevents the possibility of packing the larger residues against the gauze where they could act as a filter and prevent the pollen material from passing through the sieve meshes.

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APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT LECTURER IN HORTICULTURE and ASSISTANT WARDEN (single, male, with a university degree or diploma in horticulture and a sound knowledge of practical horticulture)—The Principal Agricultural Officer, Lancashire County Institute of Agriculture, Hutton, near Preston, Lancashire (December 28).

JUNIOR BIOCHEMIST (Basic grade) IN THE DEPARTMENT OF PATHOLOGY—The Group Secretary, Alder Hey Children's Hospital, Liverpool 12 (December 28).

LABORATORY ASSISTANT IN THE SCIENCE DEPARTMENT, to be responsible to the Head for the maintenance of the Physics Laboratories—The Principal, Acton Technical College, High Street, Acton, London, W.3, quoting W.589N (December 28).

LABORATORY TECHNICIAN, primarily for biology work involving the care of some animals—The Secretary, Furzedown College, Welham Road, London, S.W.17 (December 28).

SCIENTIFIC OFFICER (preferably graduate in science and with a knowledge of bee-keeping) at Wallaceville Research Station, to specialize in problems affecting the bee-keeping industry in New Zealand—The High Commissioner for New Zealand, 415 Strand, London, W.C.2, quoting B11/2/2 (December 31).

SENIOR and JUNIOR RESEARCH FELLOWS (with a first- or second-class honours degree in an appropriate subject and evidence of a very high standard of ability in research) at Government Scientific Establishments—The Civil Service Commission, Scientific Branch, 20 Old Burlington Street, London, W.1, quoting S.4695/57 (December 31).

SENIOR LECTURER (with a good honours degree, teaching experience, and wide industrial experience related to instrument engineering and/or electronics) IN PHYSICS, to be responsible for planning developments in the subject, more especially in the fields of applied physics allied to instrumentation—The Registrar, Flintshire Technical College, Connah's Quay, near Chester (December 31).

SCIENTIFIC OFFICER or SENIOR SCIENTIFIC OFFICER (with a first- or second-class honours degree in civil engineering or equivalent) AT THE BUILDING RESEARCH STATION (D.S.I.R.), Garston, Herts, for research on engineering design and construction of nuclear power plants, particularly in concrete and reinforced concrete—The Ministry of Labour and National Service, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting E.609/7A (January 4).

SCIENTIFIC OFFICER (with a first- or second-class honours degree in bacteriology, with biochemistry, chemistry or biology as subsidiary; or in biochemistry with bacteriology as subsidiary; and preferably some research experience in bacteriology and the ability to go to sea) AT TORRY RESEARCH STATION (D.S.I.R.), Aberdeen, to deal with problems relating to the preservation and quality of fish as food, and to lead and direct various pieces of research, some academic, some applied—The Ministry of Labour and National Service, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting G.404/7A (January 4).

LECTURER IN AGRICULTURAL CHEMISTRY (SOIL SCIENCE); and a TECHNICAL ASSISTANT IN THE DEPARTMENT OF AGRICULTURAL CHEMISTRY, Waite Agricultural Research Institute—The Registrar, University of Adelaide, Adelaide, South Australia (January 20).

LECTURER IN ELECTRICAL ENGINEERING (HEAVY)—The Secretary, The Queen's University of Belfast, Northern Ireland (January 22).

RESEARCH CHAIR OF WOOL TEXTILE ENGINEERING—The Registrar, The University, Leeds 2 (January 31).

POSTGRADUATE RESEARCH SCHOLARS IN BACTERIOLOGY, CHEMISTRY, HOUSEHOLD SCIENCE, MATHEMATICS or PHYSICS—The Secretary, Queen Elizabeth College (University of London), Campden Hill Road, London, W.8 (March 1).

ABSTRACTOR/INDEXER WITH THE AGRICULTURAL RESEARCH COUNCIL'S UNIT OF EXPERIMENTAL AGRONOMY, to assist in the production of *Weed Abstracts*—The Secretary, Department of Agriculture, Agricultural Research Council, Parks Road, Oxford.

ABSTRACTORS (preferably with a working knowledge of languages) AT THE FUEL RESEARCH STATION (D.S.I.R.), East Dulwich, to abstract world scientific literature on fuel and power—The Ministry of Labour and National Service, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.320/7A.

ASSISTANT BIOCHEMIST (with a B.Sc. degree with honours in chemistry or biochemistry, or the A.R.I.C.)—The Group Pathologist, Withington Hospital, Manchester 20.

CHEMIST OR METALLURGIST (male, with an honours degree or equivalent qualification) IN THE PHYSICAL CHEMISTRY SECTION of the Chemistry Department in the Battersea (London) Laboratories of the B.I.S.R.A., for research work on the physical chemistry of ferrous metallurgical processes—The Personnel Officer, British Iron and Steel Research Association, 11 Park Lane, London, W.1, quoting "C.P.9".

EXPERIMENTAL OFFICER (with G.C.E.(A.), H.N.C., or equivalent, and preferably with radiation dosimetry or photographic experience), to assist in the development of instruments and equipment, including contracts liaison, and to supervise the personnel monitoring film service of the Health Physics Division—The Recruitment Officer (952Z/34), Atomic Energy Research Establishment, Harwell, Didcot, Berks.

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LECTURERS, ASSISTANT OR ASSOCIATE PROFESSORS (2) IN THE DEPARTMENT OF PHYSICS—Dr. B. G. Whitmore, Chairman, Department of Physics, The University of Manitoba, Winnipeg, Manitoba, Canada.

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VISITING LECTURER IN MATHEMATICS—Prof. A. D. Wallace, Tulane University, New Orleans, La., U.S.A.

REPORTS and other PUBLICATIONS

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Institute of Navigation. Report of the Council, 1956–57. Pp. 16. (London: Institute of Navigation, 1957.) [309

Association of British Chemical Manufacturers. **A System of Labels for Gassing Casualties sent to Hospital. Second edition.** Pp. v+44. (London: Association of British Chemical Manufacturers, 1957.) 5s. [309

Radio Industry Council. Specification No. RIC/1,000/A: Choice of Materials for Radio and other Equipment and for Components therein. Pp. 31. (Issue No. 2—January, 1957.) Specification No. RIC/1,000/B: Choice of Finishes for Radio and other Electronic Equipment and for Components therein. Pp. 24. (Issue No. 2—January, 1957.) (London: Radio Industry Council, 1957.) [309

Other Countries

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Annual Report of the National Museum, Bloemfontein, for the year ended 31st March, 1957. Pp. 14+4 plates. Researches of the National Museum. Vol. 1, Part 10: The Fossil Pigs of Florisbad. By R. F. Ewer. Pp. 239–258 (4 plates). (Bloemfontein: National Museum, 1957.) [269

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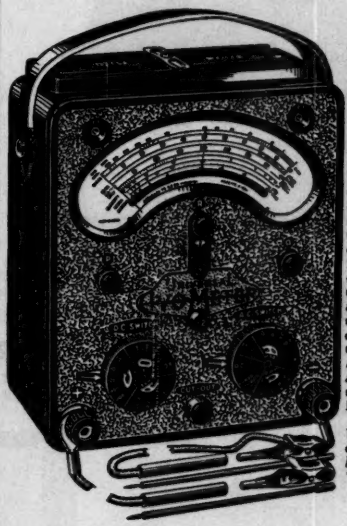

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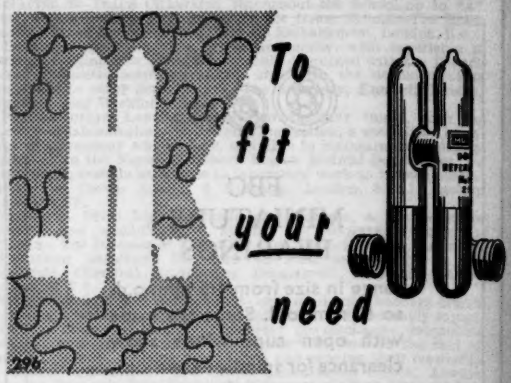

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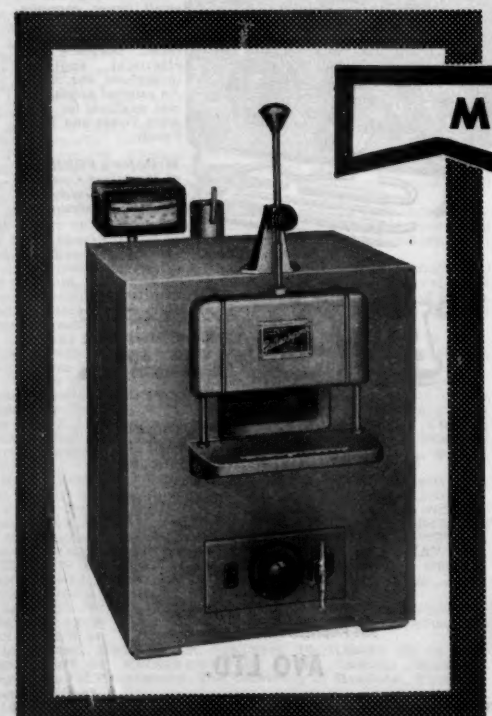

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